NBER WORKING PAPER SERIES

DO LOCAL SYNTHETIC OPIOID OVERDOSE DEATHS AFFECT PROVIDER PRESCRIBING OF BUPRENORPHINE?

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Working Paper 35648
http://www.nber.org/papers/w35648

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
August 2026

We thank Brad Stein, Adam Gordon, Harold Pollack, Alberto Ortega, Rosanna Smart, and Christine Durrance for insightful feedback on this project, as well as comments from attendees at the Spring 2026 RAND OPTIC Summit and the 2026 ASHEcon Annual Conference. Access to IQVIA Longitudinal Prescription (LRx) data was provided to the study team through a project supported by the Preparedness and Treatment Equity Coalition and Pew Trusts; we thank IQVIA for graciously providing LRx data for this project, and Pew Trusts for supporting this project. Research time for Aalsma and Siegal was supported by the National Institutes of Health through the National Institute on Drug Abuse Justice Community Opioid Innovation Network cooperative through award number UG1DA050070. Research time for Crystal was supported by NIH awards 5R01DA057568, 1R01DA058664, and 1UM1TR004789. Research time for Miles was supported by NIH K99DA057372 and R00DA057372. Research time for Pacula was supported by NIH award to OPTIC (2P50DA046351). The views expressed are those of the authors and do not necessarily represent the views of any funding agencies. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript. The views expressed herein are those of the authors and do not necessarily reflect the views of the National Bureau of Economic Research.

At least one co-author has disclosed additional relationships of potential relevance for this research. Further information is available online at http://www.nber.org/papers/w35648

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Do Local Synthetic Opioid Overdose Deaths Affect Provider Prescribing of Buprenorphine?
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NBER Working Paper No. 35648
August 2026
JEL No. I10, I12

ABSTRACT

Buprenorphine prescribing for opioid use disorder remains far below the scale of the overdose crisis. We estimate the causal effect of county-level synthetic opioid overdose mortality shocks on the volume of buprenorphine treatment delivered, exploiting the staggered geographic diffusion of synthetic opioids from 2013 to 2023. Linking IQVIA Longitudinal Prescription Claims to National Vital Statistics System mortality records, we implement a difference-in-differences estimator with propensity score matching under three complementary exposure measures. Treatment volume increases significantly under all three definitions, with no evidence of differential pre-trends; point estimates for buprenorphine prescribing rates range from 5 to 17 percent of pre-treatment means, emerge within one to two quarters, and grow monotonically thereafter. Our design does not separately identify changes in patient demand and provider behavior, but the increase in unique prescribers is consistent with a provider-side response. The response is concentrated among advanced practice providers, Medicaid patients, and counties with pre-existing buprenorphine infrastructure; counties with little baseline prescribing show no response. Local mortality information acts as a determinant of treatment volume, with effects comparable in magnitude to major legislative interventions aimed at expanding treatment, but appear only where prescribing capacity already exists.

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1 Introduction

There is often a gap between clinical best practices and observed provider behavior. Providers may under-prescribe evidence-based therapies, respond to peer norms more strongly than to clinical guidelines, and allocate effort unevenly across patients who differ in social visibility [Abaluck and Gruber, 2011, Donohue et al., 2018, King et al., 2026]. A substantial behavioral economics literature has documented these patterns, linking them to bounded rationality, inattention, and the structure of the decision environment [Adkisson, 2008, Loewenstein et al., 2012]. Yet, relatively little is known about how providers respond when community-level need becomes acutely salient. Such contexts arise when the problem they are underproviding treatment for visibly escalates around them. This paper uses the staggered geographic diffusion of synthetic opioid mortality across US counties as a case study of this question.

Buprenorphine is among the most effective pharmacotherapies for opioid use disorder (OUD), with strong evidence of reductions in mortality, illicit drug use, and criminal justice involvement, including in the fentanyl era [Mattick et al., 2014, Wakeman et al., 2020, Nunes et al., 2024, Chambers et al., 2023, Shiwach et al., 2025]. Despite surges in fentanyl and other synthetic opioid overdose deaths over the past decade, prescribing has remained far below levels commensurate with documented need. Prescribing buprenorphine to treat OUD has been limited, uneven, and concentrated in a small share of clinicians [Stein et al., 2016, Dick et al., 2015, Stein et al., 2021]. Prior work has attributed this gap primarily to supply-side frictions: regulatory barriers, training requirements, stigma, and reimbursement structure [Stein et al., 2015, Jones et al., 2015]. But an important complementary channel has received less attention: whether providers, as agents embedded in local communities, are responsive to the urgency of need around them.

Behavioral economics offers a framework for understanding this channel. Providers are not fully attentive decision-makers processing all available signals about disease burden in their communities; they are imperfectly informed, subject to salience effects, and responsive to visceral or local cues in ways that aggregate statistics do not reflect [Loewenstein et al.,

2012, Bordalo et al., 2013]. When overdose deaths become a visible local phenomenon, the proximity of the problem in a provider's decision environment shifts. This is the behavioral analog to what public health researchers call "community need," which is not merely measured prevalence, but the experienced salience of that prevalence to the providers who might act on it. If providers respond to community need in this sense, then local crisis shocks that increase the salience of OUD may be a mechanism through which treatment increases, independent of any formal policy change.

This paper provides empirical evidence on this question. We ask whether escalating synthetic opioid-driven overdose mortality in a county causes local providers to expand buprenorphine prescribing. Our estimates capture the effect of local crisis onset on the volume of buprenorphine treatment delivered in a county, which reflects both provider prescribing decisions and patient presentation for care. We present evidence bearing on the provider margin specifically, including increases in the number of unique prescribers, while acknowledging that our design does not guarantee it as the only mechanism at play. The synthetic opioid crisis provides an unusually clean setting for this question. The geographic diffusion of fentanyl and its analogues through illicit trafficking networks has been rapid, uneven, and largely independent of local socioeconomic or healthcare conditions [Powell et al., 2025, Bryce Pardo et al., 2019]. The arrival of synthetic opioids in a community constitutes a sudden, visible, and exogenous shock to local crisis severity, which providers experience in practice, not merely as a statistical report. We use this staggered arrival to identify how providers respond to abrupt, locally salient signals of unmet treatment need.

Our identification strategy exploits the staggered geographic diffusion of synthetic opioids across US counties. We construct three complementary measures of local crisis exposure, each capturing a different dimension of how synthetic opioid-driven mortality materializes in a community. The *first-occurrence* measure identifies the initial quarter in which a county records strictly more than one synthetic opioid death (i.e., at least two deaths), marking syn-

thetic opioids' arrival in the local drug supply.[1] This approach of exploiting variation in the timing of first local exposure to a health shock follows a broader methodological tradition: Shahid [2026] uses the staggered timing of first reported AIDS cases across cities to study behavioral responses, finding that the first local case produced immediate and heterogeneous changes in behavior. The *acute-escalation* measure identifies the first quarter in which synthetic opioid deaths exceed the county's own four-quarter rolling mean rate by one standard deviation, capturing sudden spikes above local baseline. Our operationalization draws on the approach of Rubalcaba et al. [2024], who used a similar within-unit deviation-from-trend measure to identify sharp local shocks in the context of immigration enforcement. Additionally, the CDC's Early Aberration Reporting System flags a health event when observed counts exceed a moving baseline mean by a multiple of its standard deviation [Hutwagner et al., 2003]. The *sustained entry* measure identifies the first incidence of three consecutive quarters each recording at least one synthetic opioid death, capturing the transition from sporadic to entrenched synthetic opioid mortality. This measure is analogous to the crack cocaine market penetration measure of Evans et al. [2016], who identified sustained crack arrival using consecutive periods of crack-related mortality.

We link IQVIA Longitudinal Prescription Claims data, aggregated to county-quarter level via HUD-USPS crosswalks, to county-level mortality from the National Vital Statistics System (NVSS) and population denominators from the Surveillance, Epidemiology, and End Results (SEER) Program. For each shock measure, treated counties are matched to not-yet- and never-treated controls using nearest-neighbor propensity score matching without replacement on pre-period prescribing levels, trends, and standard deviations. Treatment effects are estimated via the Callaway and Sant'Anna [2021] difference-in-differences estimator with doubly robust estimation, which is robust to heterogeneous treatment effects across cohorts and over time. Standard errors are clustered at the county level via bootstrap.

Our results are consistent across specifications. Across all three shock definitions, buprenor-

[1] We use the threshold of strictly more than one death (> 1, i.e., ≥ 2) rather than ≥ 1 to reduce the influence of isolated or potentially miscoded single deaths. We test sensitivity to this in Section 6.9.

phine prescribing increases significantly following local synthetic opioid crisis onset, with no evidence of differential pre-trends. The first-occurrence measure yields an average treatment effect on the treated (ATT) of 11.68 additional patients per 100,000 population (SE = 2.95, $p < 0.001$), representing a 9.98 percent increase relative to the pre-treatment mean of 117 buprenorphine patients per 100,000. The acute-escalation measure produces the smallest point estimate of 5.30 additional patients per 100,000 (SE = 2.56, $p < 0.05$). Finally, the sustained entry measure produces the largest point estimate of 23.30 additional patients per 100,000 (SE = 3.00, $p < 0.001$). Effects emerge within one to two quarters post-shock and grow monotonically over subsequent quarters, consistent with a sustained behavioral response instead of a transient adjustment. Heterogeneity analysis reveals that the response is concentrated among advanced practice providers (nurse practitioners and physician assistants), Medicaid-enrolled patients, counties with above-median baseline buprenorphine prescribing, and counties east of the Mississippi River, where synthetic opioids penetrated drug markets earliest. Counties with below-median baseline prescribing show no significant effect, suggesting the organic channel amplifies existing treatment infrastructure.

This paper contributes to three literatures. First, we contribute to the behavioral economics of provider decision-making. A growing literature documents how providers respond to information, peer norms, and non-clinical cues in ways that depart from the predictions of the standard model [Abaluck and Gruber, 2011, Donohue et al., 2018]. We provide evidence of a new such channel: responsiveness to salient local health shocks. Because our county-level outcome also reflects patient presentation, we interpret this as evidence that the provider information environment contributes to the response, supported by the prescriber-entry results, but cannot claim that provider cognition is the sole mechanism. This complements studies of how community-level context affects clinical behavior [Miles et al., 2023, Nguyen et al., 2022] and suggests that the provider's information environment, not just regulatory constraints or training, is a meaningful determinant of treatment supply. Second, we contribute to the determinants of buprenorphine prescribing and MOUD treatment provision

more broadly [Stein et al., 2016, Dick et al., 2015, Stein et al., 2021, 2015, Jones et al., 2015]. We identify community crisis severity as an organic channel through which local demand conditions activate treatment supply. Third, our strategy to exploit entry of synthetic opioids into local communities complements the work by Evans et al. [2016, 2022], Alpert et al. [2022], Donahoe and Drake [2025], by identifying why such supply-side shocks could have such persistent impacts on these markets, even as funding for treatment expanded and perceived barriers were removed. More broadly, this contributes to the literature on how illicit drug market dynamics propagate through healthcare systems [Pacula et al., 2025].

The remainder of the paper is organized as follows. Section 2 provides institutional background. Section 3 describes the data sources and variable construction. Section 4 presents the empirical strategy. Section 5 reports the main results. Section 6 presents robustness checks. Section 7 discusses the findings, and Section 8 concludes.

2 Background

2.1 Buprenorphine and the Treatment of Opioid Use Disorder

Buprenorphine is a partial opioid agonist approved by the US Food and Drug Administration in 2002 for the treatment of opioid use disorder. As a partial agonist, buprenorphine activates opioid receptors with lower intrinsic efficacy than full agonists such as heroin or fentanyl, producing a ceiling effect on respiratory depression that substantially reduces overdose risk. Clinical evidence consistently demonstrates that buprenorphine maintenance therapy reduces illicit opioid use, overdose mortality, and criminal justice involvement relative to no pharmacotherapy or to behavioral treatment alone [Mattick et al., 2014, Wakeman et al., 2020].

Until 2023, prescribers were required to obtain a Drug Enforcement Administration (DEA) waiver (commonly known as the "X-waiver") to prescribe buprenorphine for OUD, a regulatory barrier that limited the pool of eligible providers. The X-waiver requirement was

eliminated by the Consolidated Appropriations Act of 2023, effective January 2023, removing a key supply-side constraint on buprenorphine access. However, even before its elimination, the effective constraint on buprenorphine access was less the waiver itself than providers' willingness to obtain and actively use it. Stein et al. [2016] documented that physician capacity to treat OUD with buprenorphine lagged substantially behind need, and Stein et al. [2021] found that prescribing was heavily concentrated among a small share of clinicians. Understanding what motivates providers to initiate or expand buprenorphine prescribing is therefore critical regardless of the regulatory environment.

Clinical studies focused on the synthetic opioid era found that buprenorphine remains effective when patients are addicted to synthetic over prescription opioids or heroin. Although effective treatment of synthetic opioid use disorder may require higher doses than those historically used for prescription opioid or heroin addiction [Nunes et al., 2024, Chambers et al., 2023, Shiwach et al., 2025]. Chambers et al. [2023] document that higher buprenorphine doses are associated with treatment retention among patients treated in the fentanyl era, suggesting that dose-level prescribing decisions have meaningful implications for outcomes. A clinical review of the dose evidence finds dose-dependent benefits up to at least 32mg per day, including reductions in withdrawal symptoms, craving, and illicit use and improved retention in care, and documents that patients frequently faced a practical dose limit of 16 or 24mg per day derived from FDA package labeling [Grande et al., 2023]; higher daily doses have also been associated with lower urgent health care utilization [Axeen et al., 2024]. Although the labeling never established an explicit maximum, the 16mg target and the 24mg statement were widely interpreted as ceilings and were operationalized as such by insurers and some state Medicaid programs through prior authorization and quantity limits [Grande et al., 2023, Clark et al., 2014]. In December 2024, after our sample period ends, the FDA recommended labeling changes clarifying that neither 16mg nor 24mg should be interpreted as a maximum dosage and that daily doses above 24mg may be appropriate for some patients [Food and Drug Administration, 2024]. Throughout our 2013 to 2023 sample, then,

prescribing above 24mg marked a deliberate departure from the prevailing clinical anchor, which is why Section 6.2 treats the share of patients crossing the 16mg and 24mg thresholds as a candidate signature of adaptation to the synthetic opioid population. Stein et al. [2025] provide a descriptive account of higher-dose buprenorphine prescribing in this era using the same thresholds; we complement that work by estimating whether local mortality shocks cause movement across them. Expanding the number of patients receiving buprenorphine remains a clinically meaningful response to synthetic opioid mortality.

2.2 The Synthetic Opioid Crisis and Its Geographic Diffusion

The current wave of the opioid crisis is driven by synthetic opioids, which have rapidly displaced heroin and increasingly appear in the supply of other illicit substances including counterfeit prescription pills and stimulants. The geographic diffusion of synthetic opioids has followed trafficking network pathways that are largely orthogonal to local demand conditions for other opioids or local healthcare market characteristics [Bryce Pardo et al., 2019]. Powell et al. [2025] document the geographic and racial dimensions of synthetic opioids' diffusion, showing disproportionate impacts on Black communities.

The analogy to the crack cocaine epidemic is evident. Evans et al. [2022] argued that the timing of crack's arrival in US cities was driven by the expansion of trafficking networks along interstate corridors and was largely independent of local socioeconomic conditions, enabling its use as a plausibly exogenous shock for causal inference. Similarly, Fryer et al. [2013] showed that the crack cocaine index they constructed was uncorrelated with a wide range of pre-period city characteristics conditional on population and region. The synthetic opioid crisis shares this supply-side origin: synthetic opioids enter local drug markets through trafficking infrastructure whose geographic reach depends on upstream production and distribution decisions (primarily involving precursor chemicals sourced internationally and processed in Mexican laboratories) instead of local demand or healthcare capacity [Bryce Pardo et al., 2019]. We discuss threats to this assumption in detail in Section 4.2.

2.3 Provider Decision-Making and Information Salience

The behavioral economics literature has documented that salient, clear information is more likely to affect decision-making than abstract statistical summaries [Krämer, 2014]. Overdose deaths, particularly those involving synthetic opioids, are often highly visible events in a community. They may involve emergency department encounters [Vivolo-Kantor et al., 2018], media coverage, public health alerts, and coroner reports.

Several mechanisms could underlie a provider response to local overdose mortality. First, providers may directly observe the consequences of untreated OUD among their own patient panels. Doctor et al. [2018] illustrate that mortality information at the patient level can shift provider behavior when it is made salient. Using a randomized study, they find opioid prescribers directly notified of a specific patient's fatal overdose substantially reduced their high-risk opioid prescribing relative to controls. Second, institutional responses to overdose crises may create enabling conditions for expanded prescribing. Third, social and professional norms around OUD treatment may shift as the crisis evolves or hits critical levels in particular areas. Evidence from physician migration studies shows that practice norms are highly malleable and physician behavior will conform to the norms of a new practice. For example, cardiologists who relocate to areas with different treatment intensities rapidly converge toward local practice patterns [Molitor, 2018], and OBGYNs update their C-section practices in response to peer behavior, even if they do not fully revise their prior beliefs [Epstein and Nicholson, 2009]. More broadly, local area effects are themselves significant independent drivers of healthcare utilization and opioid prescribing [Finkelstein et al., 2016, 2025]. These studies suggest that community-level salience shifts can reshape professional norms. Our empirical strategy does not isolate these specific mechanisms but instead estimates the reduced-form effect of crisis exposure on prescribing behavior.

Synthetic opioid-driven overdose deaths have been shown to be qualitatively different from prior waves of opioid mortality. Unlike deaths during the prescription opioid or heroin phases of the crisis, synthetic opioid deaths frequently involve individuals with no docu-

mented history of opioid use disorder. A CDC analysis of adolescent overdose deaths from 2019 to 2021 found that while 84 percent of fatalities involved synthetic opioids, only 35 percent of decedents had a documented history of opioid use, and only 11 percent had any record of substance use treatment [Friedman et al., 2022, Tanz et al., 2022]. Illicit drug supplies are increasingly contaminated, such as synthetic opioids being pressed into counterfeit pills resembling prescription medications for anxiety, ADHD, and pain, and are mixed into cocaine and methamphetamine, exposing individuals who did not intend to consume opioids to lethal doses [Friedman and Shover, 2023, Perdue et al., 2024]. The resulting deaths therefore involve younger individuals, those without prior treatment contact, and those from demographic groups not previously associated with the opioid crisis in a given community. These changing dynamics of the affected population could heighten the signal that synthetic opioid deaths send to providers through several channels. Deaths among individuals without prior opioid use history may broaden providers' perception of who is at risk, expanding the population they view as candidates for prevention or treatment. Deaths that appear random or unintentional, such as an otherwise-healthy individual who overdoses after unknowingly taking a counterfeit pill or adulterated stimulant, may generate more community alarm and media attention than deaths among individuals with known, long-standing substance use disorders, increasing the visibility of the crisis to providers who do not specialize in addiction medicine. The contaminated-supply framing may reduce the stigma providers associate with opioid use disorder, reframing affected individuals as victims of a poisoned drug supply not as people whose behavior caused their condition. Our empirical strategy captures the reduced-form effect of crisis exposure on prescribing and cannot isolate which of these channels predominates, but the qualitative distinctiveness of synthetic opioid deaths relative to earlier crisis waves provides a conceptual foundation for why local synthetic opioid mortality may provoke a stronger provider response than prior forms of overdose mortality.

While our reduced-form design cannot isolate information salience as the sole operative mechanism, several features of the setting suggest the provider cognition channel is oper-

ative. No national clinical guidelines or federal directives specifically calling for expanded buprenorphine prescribing in response to synthetic opioid mortality were issued during our study period, making it difficult to attribute the prescribing response to compliance with a national directive. The concentration of effects among advanced practice providers and Medicaid patients is consistent with individual provider updating, though we cannot rule out that state or local institutional responses to overdose crises are themselves disproportionately targeted at the safety-net settings where advanced practice providers and Medicaid patients are concentrated. In Section 6.6, we further examine whether the content of the response reflects adaptation to the synthetic opioid population specifically, and in Section 6.10, we validate that mortality signals were accompanied by concurrent growth in public and media salience.

3 Data

3.1 Buprenorphine Prescribing

Our primary outcome measure is the number of unique patients receiving buprenorphine prescriptions per 100,000 population at the county-quarter level. We construct this measure from IQVIA Longitudinal Prescription Claims (LRx) data, which captures approximately 92 percent of all US dispensed prescriptions and includes de-identified patient and prescriber identifiers, drug product codes, quantities dispensed, and provider location. Prescriptions are mapped to counties using HUD-USPS ZIP-to-county crosswalk files.

We restrict the sample to buprenorphine formulations indicated for OUD treatment, excluding formulations used primarily for pain management (e.g., transdermal patches). Population denominators are drawn from the Surveillance, Epidemiology, and End Results (SEER) Program.

In addition to the primary outcome, we construct several secondary outcomes to decompose the prescribing response (see Section 6.1): the number of unique buprenorphine

prescribers per 100,000 population (using NPI identifiers linked to NPPES), patients per prescriber (intensive margin), and total buprenorphine prescriptions dispensed per 100,000.

Patient age is drawn directly from IQVIA's patient age field. Based on the patient-quarter mean age, we assign patients to three non-overlapping bands (18–29, 30–64, 65+) and construct population-weighted patient rates per 100,000 within each band.

3.1.1 Dosing Measures

To construct the targeted outcomes examined in Section 6.6, we derive patient-level daily buprenorphine dose from the IQVIA strength description field, which reports the milligram buprenorphine content of each dispensed unit. This field takes one of three formats: a single value for sublingual tablets and films (e.g., "8 MG"), a ratio for buprenorphine-naloxone combination products (e.g., "8-2 MG," where the first number is the buprenorphine content), and a milligram-per-milliliter value for the extended-release injectable formulations Sublocade and Brixadi (e.g., "100 MG/0.5 ML"), which are dispensed as fixed-dose prefilled syringes over daily oral doses. We take the leading numeric value in each case as milligrams of buprenorphine per dispensed unit.

Daily dose for a given prescription is calculated as milligrams per unit times units dispensed, divided by days of supply. For sublingual products, units dispensed is recorded directly (e.g., 30 films for a 30-day supply of one 8mg film daily implies 8mg/day). For the injectable formulations, the dispensed-quantity field is coded inconsistently across records as either a syringe count or a milliliter volume, with no field indicating which convention applies to a given claim. We disambiguate using the fact that a syringe cannot be fractionally dispensed: a non-integer quantity must represent milliliters and is converted to a syringe count by dividing by the milliliters per syringe implied by the strength field. Records with an ambiguous whole-number quantity of two or more syringe-equivalents (which could represent either convention) are dropped from the dosing calculations only, not from patient or age counts; this affects fewer than 0.01 percent of buprenorphine patients. We addition-

ally exclude the 0.15 percent of records implying a daily dose above 40mg, which exceeds any clinically recommended buprenorphine dosing ceiling and may reflect data errors in the recorded days-supply field.

We convert milligram doses to morphine milligram equivalents (MME) using the CDC's conversion factor of 30 for sublingual/buccal buprenorphine. No separate CDC factor exists for the depot injectable formulations, so we apply the same factor uniformly across all formulations. The patient-quarter average daily dose is the days-supply-weighted mean across all scripts filled by that patient in the quarter, so that a 90-day prescription's daily rate contributes proportionally more than a 7-day prescription's. The high-dose threshold shares (share of patients exceeding 16mg or 24mg per day) are constructed differently: instead of using the quarter-average dose, a patient is flagged as exceeding a threshold if any single script active during the quarter implies a daily dose above that threshold. This "ever-exceeded" construction is intended to capture peak dosing intensity within the quarter. These two thresholds are derived from FDA recommended targets of 16mg for buprenorphine maintenance treatment, and 24mg is the level widely interpreted as the labeled maximum [Chambers et al., 2023, Grande et al., 2023].[2]

3.2 Synthetic Opioid Crisis Exposure

We measure synthetic opioid crisis exposure using county-level mortality data from the National Vital Statistics System (NVSS) restricted-use multiple-cause-of-death files. We identify synthetic opioid deaths using ICD-10 underlying cause of death codes for drug poisoning (X40–X44, X60–X64, X85, Y10–Y14) with a contributing cause code of T40.4 (synthetic opioids other than methadone).

From these mortality counts, we construct three measures of synthetic opioid crisis exposure:

[2]These thresholds reflect FDA labeling in effect throughout our sample period. In December 2024, after our sample ends, the FDA recommended changes to buprenorphine labeling to clarify that neither 16mg nor 24mg should be interpreted as a maximum and that daily doses above 24mg may be appropriate for some patients [Food and Drug Administration, 2024]

(1) **First occurrence.** The first quarter in which a county records strictly more than one synthetic opioid overdose death (i.e., at least two deaths). As shown in Figure 1, roughly half of eventually treated US counties had crossed this threshold by 2017.

(2) **Acute escalation.** The first quarter in which synthetic opioid deaths exceed the county's own four-quarter rolling mean by one standard deviation. This construction mirrors the aberration-detection logic of CDC's Early Aberration Reporting System, which flags a health event when observed counts exceed a moving baseline mean by a multiple of its standard deviation [Hutwagner et al., 2003], so the quarters our measure flags are the same events a public health surveillance system would flag.

(3) **Sustained entry.** The first incidence of three consecutive quarters each recording at least one synthetic opioid death.

We note that these three measures are not independent. A county that experiences its first synthetic opioid deaths will, if the problem persists, eventually also experience acute escalation and sustained entry. The measures therefore identify partially overlapping sets of treated counties, though with different treatment timing. In our sample, 2,121 counties are treated under the first-occurrence definition, 2,449 under acute escalation, and 1,836 under sustained entry. Of the 2,507 counties treated under at least one definition, 1,788 (71.3%) appear as treated under all three definitions. The value of examining all three measures lies not in their independence but in the fact that each captures a different dimension of crisis exposure with different treatment timing.

3.3 Additional Data Sources

We supplement the core IQVIA and NVSS analysis with several county-level data sources used as covariates and balance characteristics. County population by age, race, and Hispanic origin comes from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. Physician counts of both primary care physicians and all physicians

are constructed from the National Plan and Provider Enumeration System (NPPES), which we aggregate to the county level annually. Uninsured rates are from the Census Bureau's Small Area Health Insurance Estimates (SAHIE); poverty rates and median household income are from the Census Bureau's Small Area Income and Poverty Estimates (SAIPE). County-level retail opioid dispensing rates come from the CDC Opioid Dispensing Rate Maps, available for 2006–2023, which we use both as a balance covariate and, in Section 7.3, as a secondary outcome. These data report opioid prescriptions dispensed from retail pharmacies per 100 residents per year at the county level, derived from IQVIA Xponent. As an outcome, we restrict the analytic sample to 2013–2023 to match the coverage window of our main prescribing outcome. Two features of the series are relevant for its use as an outcome. First, it is a prescription count rather than a dose-weighted measure, so a shift toward shorter or lower-dose prescriptions would not be measured; no continuous county-year series of morphine milligram equivalents is publicly available to our knowledge. Second, it is annual rather than quarterly, so for this outcome we collapse each shock definition to the calendar year of treatment onset. Hospital bed capacity is measured as licensed beds per 1,000 population, constructed from the CMS Provider of Services (POS) December snapshots. The Rural-Urban Continuum Code (RUCC) is from the USDA Economic Research Service 2023 vintage. A binary indicator for the presence of an interstate highway is constructed from U.S. Census Bureau TIGER/Line road shapefiles accessed via the `tigris` R package [Walker, 2016].

Policy and other opioid related control variables are derived from a variety of sources and prior studies. ACA Medicaid expansion adoption dates are from the Kaiser Family Foundation. Must-access PDMP requirements are from the National Alliance for Model State Drug Laws (`www.namsdl.org`) and the Prescription Drug Abuse Policy System (`www.pdaps.org`). Marijuana legalization dates follow Anderson and Rees [2023]. Naloxone access law and Good Samaritan law provisions are from the Prescription Drug Abuse Policy System (`www.pdaps.org`). Nurse practitioner full practice authority for 2012–2019 follows the state clas-

sification in Ryskina et al. [2024]; we extend this through 2022 with independently sourced state legislative effective dates for five states outside their study sample (Alaska, the District of Columbia, Illinois, Minnesota, and New York) and for two states that adopted full practice authority after their 2019 cutoff (Massachusetts, 2021; Kansas, 2022). Florida's 2020 autonomous-practice law is not coded as full practice authority because it is conditional on specialty (primary care only) and ongoing supervised-hours and coursework requirements; New York is coded as restricted throughout because its experienced-nurse-practitioner exemption never amounted to unconditional full practice authority, consistent with Ryskina et al. [2024]'s own exclusion of New York from their classification. See Spetz et al. [2019] for the relationship between state scope-of-practice restrictions and nurse practitioner buprenorphine waivers specifically. Triplicate prescription program states follow Alpert et al. [2022]. The 1996 county cancer mortality split follows Arteaga and Barone [2026]. The east/west Mississippi River classification (a longitude cutoff at $-91°$ applied to county centroids) follows Donahoe and Soliman [2025].

3.4 Sample Construction

Our analysis sample spans 2013Q1 through 2023Q4. For each shock definition, we exclude counties whose treatment quarter under that definition falls in 2011 or 2012, as these counties are always-treated units that lack a pre-treatment period in our prescribing data. As shown in Table 1, the panel is balanced at the county-quarter level, comprising 143,500 county-quarter observations across 2,990 unique counties. Of these, 2,121 counties are treated under the first-occurrence definition, 2,449 under acute escalation, and 1,836 under sustained entry; of the 2,507 counties treated under at least one definition, 1,788 (71.3 percent) are treated under all three.

Table 1: Summary Statistics

	Mean	SD	Min	Max
Panel A: Full Sample				
Buprenorphine patients per 100,000	233.89	502.52	0.00	14,156.09
Unique buprenorphine prescribers per 100,000	9.25	14.11	0.00	339.37
Synthetic opioid deaths per 100,000	2.12	4.38	0.00	181.65
County population (thousands)	109.68	340.15	0.56	10,127.13
County-quarter observations		143,500		
Unique counties		2,990		
Panel B: Treatment Timing and Overlap				
Counties treated (first occurrence)		2,121		
Counties treated (acute escalation)		2,449		
Counties treated (sustained entry)		1,836		
Counties treated under all three definitions		1,788		
Counties never treated under any definition		483		
Median treatment quarter (first occurrence)		2017 Q1		
Median treatment quarter (acute escalation)		2016 Q1		
Median treatment quarter (sustained entry)		2018 Q1		

Notes: Panel A reports summary statistics for the full county-quarter analysis sample, 2013Q1–2024Q4 (mortality-based treatment timing extends through 2023Q4; 2024 quarters are outcome-only). Panel B reports the number of counties meeting each treatment definition and the degree of overlap.

4 Empirical Strategy

4.1 Identification

Our identification strategy exploits the staggered geographic diffusion of synthetic opioids across US counties. The Callaway-Sant'Anna estimator requires two identifying assumptions. First, conditional parallel trends: absent treatment, the evolution of buprenorphine prescribing in treated counties would have paralleled that in the comparison group, conditional on observable pre-treatment characteristics. The supply-side origin of synthetic opioid diffusion, driven by trafficking network decisions and not local healthcare market conditions, is the basis for our claim about the exogeneity of treatment timing. This is a claim about assignment, not by itself evidence that prescribing trends would have been parallel absent treatment. The empirical evidence for parallel trends is the event-study plots showing no visual evidence of differential pre-trends, formal balance tests on a rich set of county characteristics (Section 4.2), and several robustness exercises (Section 6). A related threat to parallel trends is that providers in counties with established heroin or prescription opioid markets may have had a delayed prescribing response that coincided with synthetic opioid arrival; we discuss this concern and our empirical response in Section 4.2 and Section 6.6.

Second, no anticipation: counties do not adjust buprenorphine prescribing in anticipation of imminent shock onset. This assumption is more delicate than in settings with a specific policy date because our mechanism holds that providers respond to real-time death observation instead of to our defined threshold itself. A county's first-occurrence quarter, defined as the first quarter with more than one death, can be preceded by an earlier, isolated death that providers may already have observed. We therefore do not rely on an a priori argument that anticipation is impossible, and instead assess it empirically. Event-study coefficients show no elevation in the quarters immediately preceding the coded treatment quarter under any of the three shock definitions, which is the observable signature a response to sub-threshold deaths would produce. Regional awareness of the approaching fentanyl wave preceding local

deaths is a distinct concern, addressed directly in the spatial spillover analysis (Section 6.3).

4.2 Threats to Identification

While the supply-side origin of synthetic opioid diffusion motivates our identification strategy, several threats to the exogeneity of treatment timing warrant discussion. Our method does not allow us to claim that synthetic opioid arrival is random with respect to local drug market conditions. Fentanyl entered established heroin distribution networks first, so counties treated earlier under any of our definitions differ systematically from those treated later, a pattern visible in the balance analysis below. Our claim is narrower: conditional on pre-period buprenorphine prescribing levels and trends and on observable county characteristics, the timing of local mortality escalation is driven primarily by upstream production and distribution decisions; it is not by contemporaneous changes in local treatment demand.

Two features of the treatment variable are worth pointing out. First, we observe deaths, not fentanyl itself arriving, and deaths reflect both the presence of synthetic opioids in the local supply and the size of the local population at risk. Counties with larger populations using opioids therefore cross a given threshold sooner, so treatment timing partly indexes local prevalence. Second, because our primary definitions use death counts, larger counties cross thresholds earlier for arithmetic reasons alone, which is consistent with the population imbalance reported in Tables 2, A1, and A2. Section 6.9 addresses the second concern directly by re-estimating on rate-based thresholds, which yield positive and significant estimates. The first concern is not fully separable from the mechanism itself, since a larger at-risk population will both generate deaths and generate treatment demand.

Accordingly, we interpret our estimates as the effect of local synthetic opioid crisis onset on the volume of buprenorphine treatment delivered in a county. This quantity reflects both providers' willingness to prescribe and patients' presentation for care, and our design does not separate them. Section 6.1 and Section 7.3 present evidence bearing on the provider margin specifically, which we regard as only suggestive.

Trafficking Networks and Pre-Existing Drug Market Infrastructure

Synthetic opioids do not arrive in communities at random. Rather, they enter local drug markets through trafficking infrastructure that builds on pre-existing heroin distribution networks, interstate highway access, and proximity to major distribution hubs [Bryce Pardo et al., 2019, Ciccarone, 2019]. Communities with established heroin markets may be both earlier recipients of synthetic opioids and places where OUD treatment demand, and potentially buprenorphine prescribing, were already evolving. If counties with more developed illicit drug markets also had steeper pre-existing trends in buprenorphine prescribing for reasons unrelated to synthetic opioids (e.g., because the same underlying opioid crisis was simultaneously generating demand for treatment and attracting synthetic opioid supply), our estimates could be confounded.

We address this concern in three ways. First, our matching procedure conditions on pre-period buprenorphine prescribing levels and trends, directly accounting for the possibility that early-treated counties were on different prescribing trajectories. Second, the event-study plots provide a visual test for differential pre-trends. Third, we present formal balance tables for each shock definition (Tables 2, A1, and A2) that examines whether the timing of synthetic opioids' arrival is correlated with a rich set of county characteristics beyond those used in matching.

This concern is analogous to those addressed by Evans et al. [2022] in the context of crack cocaine. Evans et al. argued that while crack arrived earlier in larger cities with existing drug market infrastructure, the timing of crack's arrival within city-size categories was plausibly exogenous to local conditions. Similarly, Fryer et al. [2013] showed that the crack index they constructed was uncorrelated with a wide range of pre-period city characteristics conditional on population and region. We adopt a parallel approach: conditional on our matching variables, we test whether the timing of synthetic opioid's arrival is associated with a broader set of county-level characteristics.

A related identification concern is that providers in counties with established heroin or

prescription opioid markets may have had a delayed prescribing response that coincided with synthetic opioid arrival, producing a spurious correlation between the synthetic opioid shock and prescribing. The balance tables (Tables 2, A1, and A2) show that treated and matched control counties are well-balanced on pre-treatment heroin death rates and opioid prescription rates, reducing the likelihood that differential pre-existing drug market conditions drive the effect. We address this further in Section 6.6: a delayed prescribing response would manifest in standard-dose prescribing for established patients, while adaptation to the synthetic opioid population might manifest in higher doses or a shift in the age composition of treated patients base. As reported there, we find limited evidence of dose escalation and a response concentrated among working-age and not younger patients, so this exercise does not resolve the concern and we treat it as one piece of descriptive evidence.

Balance on County Characteristics

Table 2 presents balance on a rich set of county characteristics for the first occurrence shock, comparing treated and matched control counties.

Most covariates exhibit adequate balance, with normalized differences below 0.25 in absolute value [Imbens and Rubin, 2016]. However, treated counties are notably more urban (normalized difference of -0.47 on Rural-Urban Continuum Code) and larger (0.62 on log population). The urbanicity and population imbalances are expected given that synthetic opioids arrived earlier in larger, more connected communities, paralleling the pattern Evans et al. [2022] documented for crack cocaine. To assess sensitivity, we estimate an augmented specification that includes Rural-Urban Continuum Code in the doubly robust step. Our main specifications also control for population. The results are robust to these various estimations as shown in Figure A4. Analogous tables and figures are presented for the other shocks in Appendix B.

Table 2: Balance on County Characteristics: Treated vs. Matched Control Counties

	Treated		Control		Norm.
	Mean	SD	Mean	SD	Diff.
Matching variables					
Pre-period mean Bup. patients/100K	192.57	321.22	187.71	315.02	0.011
Pre-period Bup. prescribing trend	5.97	45.20	4.85	36.14	0.019
Pre-period Bup. prescribing SD	30.11	61.63	28.28	52.98	0.022
Healthcare market characteristics					
Total physicians per 100,000	161.16	204.20	147.62	257.47	0.041
Primary care physicians per 100,000	76.55	73.79	77.42	105.42	-0.007
Opioid Rx rate per 100	67.41	44.15	65.35	49.90	0.031
Hospital beds per 1,000 population	5.15	6.17	6.96	8.35	-0.175
Socioeconomic characteristics					
Log population	10.59	0.95	9.76	0.96	0.616
Percent non-Hispanic Black	10.93	15.17	9.80	15.76	0.052
Percent Hispanic	8.42	12.22	9.02	12.84	-0.034
Percent age 18–44	30.22	4.07	29.06	4.19	0.198
Poverty rate (%)	15.62	5.74	16.09	6.58	-0.054
Uninsured rate (%)	11.99	4.58	13.38	5.18	-0.199
Median household income ($)	52,859.66	13,539.84	50,847.10	12,989.18	0.107
Pre-existing drug market indicators					
Rural-Urban Continuum Code	4.64	2.64	6.34	2.52	-0.466
Heroin death rate per 100,000	0.18	0.44	0.07	0.33	0.194
Non-synthetic drug OD rate per 100,000	2.52	2.44	2.02	2.45	0.143
Interstate highway within county (0/1)	0.50	0.50	0.34	0.47	0.230

Notes: Balance presented for the first-occurrence shock definition. Normalized differences calculated as the difference in means divided by the square root of the sum of variances. Values below 0.25 in absolute value are generally considered adequate balance [Imbens and Rubin, 2016]. Healthcare market characteristics are from NPPES (physician counts), the CDC Opioid Dispensing Rate Maps (opioid dispensing rate), and the CMS Provider of Services file (hospital beds per 1,000 population). Socioeconomic characteristics are from SEER (population, race/ethnicity and age shares), Census SAIPE (poverty rate and median household income), and Census SAHIE (uninsured rate). The Rural-Urban Continuum Code is from the USDA Economic Research Service. Pre-existing drug mortality rates are from NCHS mortality microdata. The interstate highway indicator is constructed from U.S. Census Bureau TIGER/Line Shapefiles.

Contemporaneous Shocks

Even with parallel pre-trends and good balance on observables, we cannot rule out the possibility that synthetic opioids arrival in particular counties coincides with other shocks that independently affect buprenorphine prescribing. For example, state-level policy changes (naloxone access laws, Good Samaritan laws, Medicaid expansion, must-access prescription drug monitoring programs), federal regulatory changes (X-waiver elimination in 2023), or local public health campaigns could be correlated with synthetic opioids' arrival timing if policymakers respond to the same crisis. Our doubly robust estimator adjusts for observable covariates, but time-varying confounders that coincide with synthetic opioids' arrival at the county level remain a potential concern. We note that the parallel trends test helps but cannot rule out confounders that coincide precisely with treatment onset.

We address this first by directly controlling for state-level policies as time-varying covariates and examine treatment effect heterogeneity by policy environment, testing whether the prescribing response differs between states with and without these policies in place at the time of treatment (Section 6.7). We then test robustness to restricting the sample to the pre-2020 period, before the X-waiver elimination and widespread use of telehealth (Section 6.5). As a placebo test, we examine whether sudden rises in other deaths produce similar prescribing responses (Section 6.8).

4.3 Matching

For each of the three shock measures, we match treated counties to not-yet- and never-treated control counties using nearest-neighbor Mahalanobis distance matching within a propensity-score caliper of 1 standard deviation, where the propensity score is estimated via logistic regression of treatment on: (i) pre-period mean buprenorphine prescribing, (ii) pre-period linear trend in prescribing, and (iii) pre-period standard deviation of prescribing. Distance within the caliper is measured using the Mahalanobis metric on the same three covariates.

We acknowledge that the current matching variables are drawn from the outcome data

rather than from structural determinants of prescribing such as physician density, rural-urban classification, or insurance coverage. This is a limitation: achieving balance on prescribing levels and trends does not guarantee balance on underlying determinants. Table 2 addresses this directly. For any systematic differences on structural determinants revealed by the balance analysis, we test our model to control for such differences. A distinct concern is that matching on pre-period outcome levels can itself introduce regression-to-the-mean bias into difference-in-differences estimates when treatment assignment is unrelated to outcome levels [Daw and Hatfield, 2018]. Two features of our setting limit this risk: county-quarter prescribing is highly serially correlated, the case in which Daw and Hatfield [2018] show the bias is smallest, and the flat, overlapping pre-treatment paths of treated and matched control counties (Figures A1–A3) are inconsistent with the transitory-shock selection that generates the bias. As a direct check, Appendix Figure A7 and Table A9 re-estimate the main specifications on the unmatched sample using the Callaway–Sant'Anna estimator with covariate adjustment only. The unmatched estimates are substantially larger and less precise than the matched estimates, indicating that matching plays an identifying role here rather than serving only as a precision refinement. Appendix Table A10 compares matched controls to the full not-yet-treated pool on the same covariates as Table 2 and finds the never-treated pool is systematically smaller, more rural, and less prescribing-intensive at baseline than the counties matching selects. We accordingly present the matched estimates as our main results for two design-based reasons. First, the unmatched pool fails the comparability that the parallel-trends assumption requires, as the never-treated counties are systematically smaller, more rural, and less prescribing-intensive at baseline than treated counties, so their counterfactual trend is unlikely to be informative for treated counties. Second, the identifying assumption has observable support only in the matched design, given that the matched samples exhibit flat, overlapping pre-treatment paths (Figures A1–A3), whereas the unmatched event studies show a downward pre-period drift under two of the three definitions (Appendix Figure A7). We retain the unmatched estimates in the appendix for transparency, and we

address residual imbalance on population and urbanicity within the matched design by showing the estimates are stable when each unbalanced covariate is added to the doubly robust step (Figure A4).

4.4 Estimation

We estimate treatment effects using the Callaway and Sant'Anna [2021] difference-in-differences estimator, which addresses the well-documented biases that can arise from two-way fixed-effect (TWFE) estimation in staggered adoption designs [Goodman-Bacon, 2021, Sun and Abraham, 2021, De Chaisemartin and D'Haultfœuille, 2020]. The estimator proceeds in two steps.

First, for each treatment cohort g and each post-treatment period t, a group-time $ATT(g,t)$ is estimated using a doubly robust estimator:

$$ATT(g,t) = E\left[\left(\frac{G_g}{E[G_g]} - \frac{\frac{\hat{p}_g(X)(1-G_g)}{1-\hat{p}_g(X)}}{E\left[\frac{\hat{p}_g(X)(1-G_g)}{1-\hat{p}_g(X)}\right]}\right)(Y_t - Y_{g-1} - m_{g,t}(X))\right] \tag{1}$$

where G_g indicates membership in cohort g, $\hat{p}_g(X)$ is the estimated propensity score, Y_t is the outcome at time t, $m_{g,t}(X)$ is the outcome regression function, and $X = \log(\text{population})$. The doubly robust property ensures consistency if either the propensity score model or the outcome regression model is correctly specified.

Second, group-time ATT estimates are aggregated to event time using cohort-size weights:

$$ATT(e) = \sum_g \frac{N_g}{\sum_{g'} N_{g'}} \cdot ATT(g, g+e) \tag{2}$$

Standard errors are clustered at the county level via 5,000 bootstrap iterations.[3]

[3]With 2,555 to 2,913 county-level clusters (varying by shock definition) and 5,000 bootstrap iterations, we assess inference adequacy by examining bootstrap CI stability. We additionally check sensitivity to the matching caliper and to clustering standard errors at the state rather than county level; see Appendix Section D.

4.5 Comparison Group

The comparison group consists of not-yet- and never-treated counties matched via the propensity score procedure described above. A practical concern is that the pool of comparisons shrinks over time. By the end of 2022, the cumulative share of treated counties exceeds 90 percent under all three shock definitions (Figure 1), leaving relatively few valid comparisons for late cohorts. Additionally, 25-43 percent of treated counties fail to match within the caliper across definitions, with unmatched counties having lower average population compared to matched counties, suggesting our estimates generalize primarily to larger, more urban counties experiencing synthetic opioid crises. Table 3 reports the number of available comparison counties by cohort for the first occurrence shock measure (Tables A3 and A4 present the analogous numbers for the other shock measures). As a robustness check, we examine whether results are sensitive to excluding late cohorts (Section 6.5).

Table 3: Comparison Group Size by Treatment Cohort

Cohort Year	Treated Counties	Available Comparisons	Matched Controls
2013	75	2303	71
2014	156	2179	149
2015	157	2003	147
2016	175	1822	148
2017	191	1665	168
2018	139	1557	126
2019	110	1377	96
2020	204	1172	169
2021+	447	3648	384

Notes: Reported for the first-occurrence shock definition.

5 Results

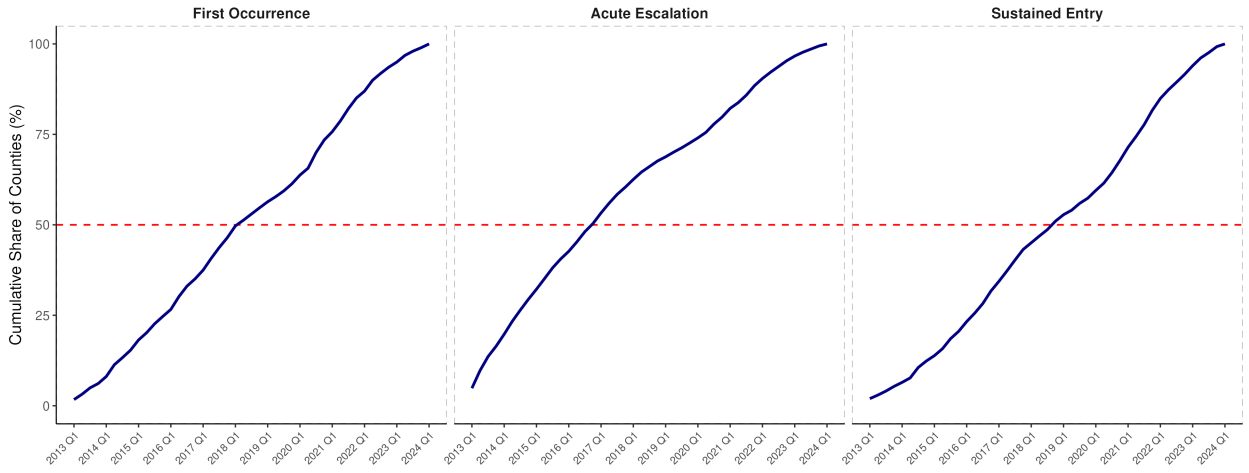
5.1 Temporal Diffusion of Synthetic Opioids

Figure 1 documents the staggered temporal diffusion of synthetic opioids across US counties, separately for each shock definition. Diffusion speed differs meaningfully across definitions: the acute-escalation measure reaches 50 percent of eventually-treated counties by 2016 Q4, versus 2018 Q2 for first occurrence and 2018 Q4 for sustained entry. This ordering follows directly from each definition's construction, as acute escalation flags any quarter exceeding a county's own rolling baseline by one standard deviation, which can trigger early off a low baseline, while sustained entry requires three consecutive qualifying quarters to accumulate. The by-year panel shows a correspondingly large early surge for acute escalation (343 counties first qualify in 2013 alone, versus 104 for first occurrence and 87 for sustained entry) and a secondary rise around 2020–2021 across all three definitions, consistent with pandemic-era acceleration of the fentanyl crisis, before mechanically declining as the pool of not-yet-crossed counties shrinks.

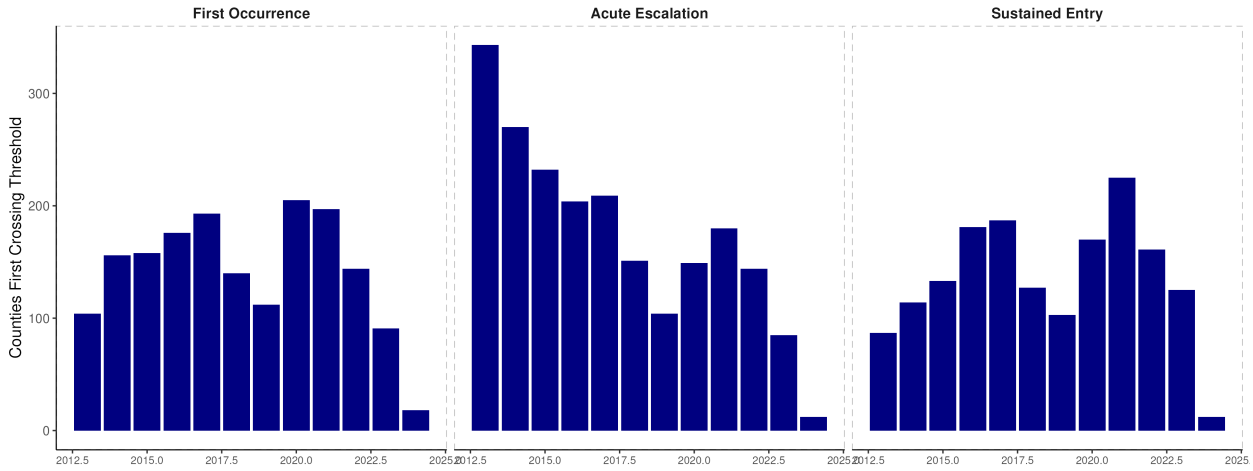
Tables 3, A3, and A4 report comparison group sizes by treatment cohort for each shock definition. For first occurrence (Table 3), the comparison pool remains adequate through the sample period. Across definitions, 57 to 75 percent of treated counties find a match within the caliper. Unmatched counties tend to be smaller and more rural, suggesting our estimates generalize primarily to larger counties. These differences in comparison pool depletion motivate the robustness check excluding late cohorts (Section 6.5).

5.2 Main Event-Study Results

Figure 2 presents event-study estimates. Across all specifications, there is no evidence of differential pre-trends, and buprenorphine prescribing increases significantly following local synthetic opioid entry onset. The acute-escalation measure produces the smallest point estimate, while the sustained-entry measure yields the largest effect, consistent with providers



(a) Cumulative Share of Eventually-Treated Counties



(b) Counties First Crossing the Threshold, by Year

Figure 1: Geographic Diffusion of Synthetic Opioid Mortality Across US Counties, 2013–2023, by Shock Definition

Notes: Data from NVSS mortality files, 2011–2023. Counties first crossing a given shock's threshold in 2011–2012 are excluded from that panel, consistent with the regression sample. Treatment quarter is coded as one quarter after the qualifying death is observed, so a small number of counties whose qualifying death occurred in 2023 Q4 appear as first crossing in 2024 Q1. Cumulative share is out of counties ever crossing that shock's threshold.

responding most strongly when synthetic opioid mortality becomes entrenched rather than sporadic.

5.3 Average Treatment Effects

Table 4 presents the aggregate ATTs. The first-occurrence measure yields an ATT of 11.68 additional buprenorphine patients per 100,000 population (SE = 2.95, $p < 0.001$), representing a 9.98 percent increase relative to the pre-treatment mean of 117 patients per 100,000. The acute-escalation measure produces the smallest point estimate at 5.30 (SE = 2.56, $p < 0.05$), a 5.10 percent increase from a pre-treatment mean of 104. The sustained-entry measure yields the largest effect at 23.30 additional patients per 100,000 (SE = 3.00, $p < 0.001$), a 17.01 percent increase from a baseline of 137.

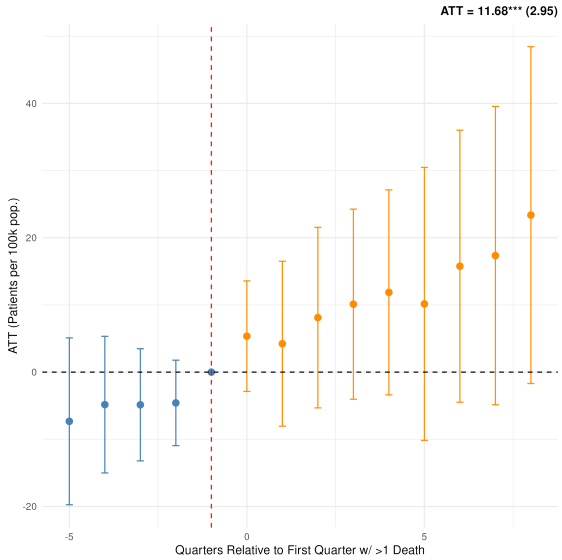
Table 4: Average Treatment Effect on the Treated: Buprenorphine Patients per 100,000

	(1) First Occurrence	(2) Acute Escalation	(3) Sustained Entry
ATT	11.68***	5.30*	23.30***
	(2.95)	(2.56)	(3.00)
Pre-treatment mean	117	104	137
Percent effect	9.98%	5.10%	17.01%
Treated counties	1654	1968	1578
Comparison counties	932	945	977
County-quarter obs.	158,740	188,872	151,468
Estimator	Callaway–Sant'Anna (2021), doubly robust		
SE clustering	County, 5,000 bootstrap iterations		

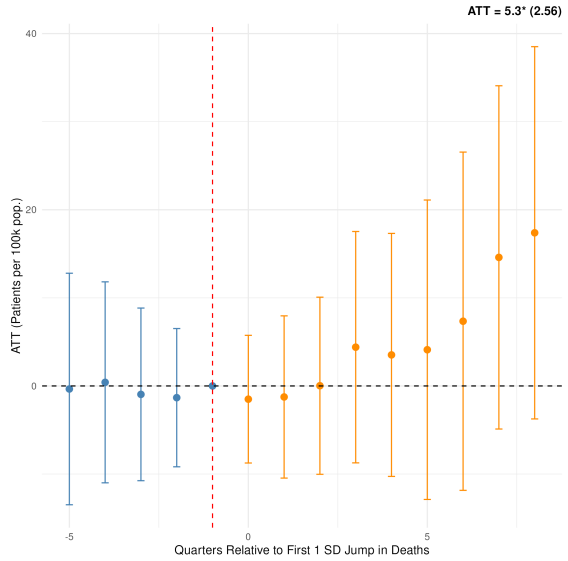
Notes: $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

Estimates are consistent across all three shock definitions, though we caution that the three measures identify substantially overlapping sets of treated counties (Table 1, Panel B). The value of the multi-measure approach is that each captures a different dimension of crisis exposure with different treatment timing.

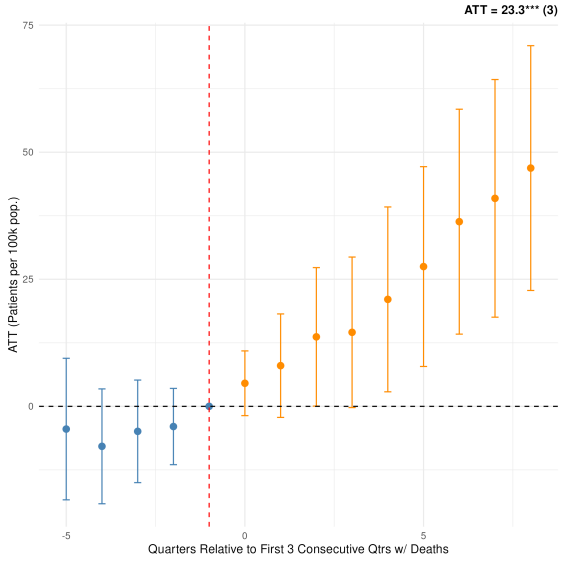
The monotonic growth of effects over event time is difficult to reconcile with a transient



(a) First Occurrence



(b) Acute Escalation



(c) Sustained Entry

Figure 2: Event-Study Estimates: Effect of Synthetic Opioid Crisis Exposure on Buprenorphine Patients per 100,000

Notes: Callaway–Sant'Anna (2021) DiD with doubly robust estimation. Blue = pre-treatment; orange = post-treatment. Bars = 95% CIs. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

adjustment and instead suggests durable behavioral change among providers.

Contextualizing Effect Magnitudes

To assess economic significance, we benchmark the effects against several reference points. We compare the magnitude to policy interventions that directly targeted buprenorphine prescribing. Following federal changes under CARA 2016, which raised the patient limit for buprenorphine-waivered providers from 100 to 275, buprenorphine dispensing increased 9.1 percent nationally from 2017 to 2018 [Roehler et al., 2020]. Medicaid expansions implemented in 2019–2023 were associated with a 21 percent increase in all-payer buprenorphine dispensing [Siegal et al., 2026]. Our estimated effects of 5 to 17 percent relative to pre-treatment means (5.30 to 23.30 patients per 100,000 on baselines of 104 to 137) are therefore comparable to these major legislative interventions, arising through an organic behavioral channel without any formal policy change.

We select CARA 2016 and Medicaid expansion as benchmarks because both have well-identified, directly measured effects on buprenorphine dispensing. Other policy changes plausibly relevant to this period, including the 2023 elimination of the X-waiver requirement and the Communities That HEAL initiative, are harder to use as comparison points because their own effects on prescribing are small or statistically indistinguishable from zero. The Communities That HEAL trial, a large, resource-intensive intervention across 67 high-overdose communities, did not significantly increase the share of clinicians actively prescribing buprenorphine [Stopka et al., 2024], underscoring that even substantial, deliberately targeted interventions do not reliably move prescribing behavior. Against that backdrop, an organic response of the magnitude we document is not a foregone conclusion.

These benchmarks speak to the magnitude of our effects relative to other interventions, but not to whether the response is proportionate to the magnitude of the underlying shock itself, since our exposure measures are binary. The acute-escalation definition offers the closest approximation to a continuous treatment intensity, since it identifies a shock scaled

to each county's own local mortality baseline. A one-standard-deviation local mortality escalation is associated with a 5.10 percent increase in buprenorphine patients per 100,000, the smallest of our three point estimates. This magnitude is modest relative to the severity of the underlying mortality escalation that defines the threshold, suggesting that short-run treatment supply responds to local crisis salience but falls considerably short of what proportional adjustment to the scale of the need would imply.

The pre-treatment mean of 117 patients per 100,000 among first-occurrence treated counties in the regression sample is somewhat below the national all-period average of 233.9, reflecting both secular growth in buprenorphine prescribing over the sample period and compositional differences across county types. The sustained-entry regression sample's own pre-treatment mean of 137, lower than the 185.5 figure, reflects the exclusion of very early-treated cohorts, which have no pre-period and cannot be matched, from the matched analysis.

5.4 Matching Diagnostics

Figures A1–A3 in the Appendix present matching performance diagnostics for each shock definition. In all three cases, treated and matched control counties follow closely parallel pre-treatment trends in buprenorphine prescribing, with the two series overlapping within confidence bands in each pre-period quarter.

Tables 2, A1, and A2 present covariate balance for each shock definition. The three matching variables are near-perfectly balanced across all specifications (normalized differences below 0.025). The main residual imbalances are on log population and the Rural-Urban Continuum Code: treated counties are larger and more urban than their matched controls. These differences reflect the fact that sustained fentanyl mortality tends to emerge first in more populous, better-connected counties. Figures A4–A6 show that the ATT estimates are stable across specifications that add each unbalanced covariate as a regression control, indicating that the residual imbalance does not account for the main results. Comparison pools remain large throughout the sample period (Tables 3 , A3, and A4).

6 Robustness and Extensions

6.1 Outcome Decomposition

Our primary outcome conflates several margins of adjustment. To disentangle the sources of the prescribing response, we estimate effects on: (i) unique buprenorphine prescribers per 100,000 (extensive margin), (ii) patients per prescriber (intensive margin), (iii) new provider entry, and (iv) total buprenorphine prescriptions per 100,000.

Table 5 presents these results. For the first-occurrence measure, both the number of unique prescribers (0.55, SE = 0.14, a 7.5 percent increase relative to the pre-treatment mean) and patients per prescriber (1.40, SE = 0.46, +5.0 percent) increase significantly, indicating that the response operates on both margins. Total prescriptions per 100,000 increase by 51.14 (SE = 13.74), a 6.5 percent increase. The pattern differs somewhat across shock definitions: under acute escalation, the extensive margin (new prescribers) and new provider entry drive the response, while the intensive margin (patients per prescriber) is not significant. Under sustained entry, the intensive margin dominates while the extensive margin has a smaller effect. This variation suggests that different dimensions of crisis exposure may activate different provider responses. Sudden spikes may prompt new providers to begin prescribing, while sustained mortality may encourage existing prescribers to expand their panels.

Table 5: Outcome Decomposition: Extensive vs. Intensive Margins

	(1) Unique Prescribers	(2) Patients per Prescriber	(3) New Provider Entry	(4) Total Rx per 100K
Panel A: First Occurrence				
ATT	0.55***	1.40**	0.08*	51.14***
	(0.14)	(0.46)	(0.04)	(13.74)
Pre-treatment mean	7.47	27.73	1.10	785.37
Percent effect	7.39%	5.04%	7.71%	6.51%
Panel B: Acute Escalation				
ATT	0.41***	-0.58	0.18***	38.2***
	(0.09)	(0.41)	(0.05)	(8.82)
Pre-treatment mean	6.23	25.18	1.38	577.17
Percent effect	6.55%	-2.29%	12.70%	6.62%
Panel C: Sustained Entry				
ATT	0.37***	2.14***	0.09*	109.24***
	(0.08)	(0.42)	(0.04)	(13.74)
Pre-treatment mean	8.26	30.14	1.15	915.76
Percent effect	4.48%	7.09%	7.95%	11.93%

Notes: $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

6.2 Population Denominator Effects

To assess whether population changes mechanically drive the per-capita results, Table 6 estimates the effect of synthetic opioid shocks on county population and on prescriptions per active provider. Column (1) shows that treated counties experience a small but statistically

significant increase in log population of 0.32 percent following a shock, rejecting the hypothesis that selective out-migration inflates the per-capita buprenorphine rate. Column (2) confirms this showing the population growth rate is economically and mostly statistically negligible. Column (3) addresses the denominator concern from the opposite direction, replacing the population base with the count of active buprenorphine providers. Prescriptions per provider rise by 5.36 following a first occurrence shock, a 4.9 percent increase relative to the pre-treatment mean, consistent with the main per-capita finding and indicating that the response reflects increased prescribing intensity instead of a mechanical artifact of the population denominator.

Table 6: Population Denominator Effects

	(1) ln(Population)	(2) Population Growth Rate	(3) Prescriptions per Provider
Panel A: First Occurrence			
ATT	0.0032***	-0.0001	5.36**
	(0.0005)	(0.0003)	(2.08)
Panel B: Acute Escalation			
ATT	0.0044***	0.0005	-0.61
	(0.0005)	(0.0003)	(1.60)
Panel C: Sustained Entry			
ATT	0.0052***	0.0006*	7.93***
	(0.0005)	(0.0003)	(1.76)
Estimator	Callaway–Sant'Anna (2021), doubly robust		
SE clustering	County, 5,000 bootstrap iterations		

Notes: Annual population measures and quarterly prescribing. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

6.3 Spatial Spillovers

If synthetic opioid mortality in one county prompts providers in neighboring counties to expand prescribing, using neighboring not-yet-treated counties as controls would attenuate our estimates. Given the well-documented geographic clustering of synthetic opioid diffusion along trafficking corridors [Bryce Pardo et al., 2019], this spillover concern is plausible.

We examine spillovers in two ways. First, we test whether prescribing increases in counties adjacent to treated counties that have not themselves experienced a synthetic opioid shock. Second, we re-estimate using non-adjacent not-yet-treated counties as the comparison group.

Table 7: Spatial Spillovers

	First occurrence	Acute escalation	Sustained entry
Panel A: Spillover — neighbor-treated counties			
ATT	-1.9	5.64**	5.04
	(3.33)	(2.17)	(2.88)
Panel B: Non-adjacent clean controls			
ATT	18.52***	16.88***	17.63***
	(2.83)	(3.04)	(3.92)
Estimator	Callaway–Sant'Anna (2021), doubly robust		
SE clustering	County, 5,000 bootstrap iterations		

Notes: Outcome is buprenorphine patients per 100,000 population. *Panel A*: treated counties are those whose first neighbor shock precedes their own. *Panel B*: same treated counties as the main analysis; potential controls bordering any county treated within ±4 quarters of cohort g are excluded and matching is re-run on the restricted pool. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

We find little evidence that prescribing increases in counties adjacent to shocked counties prior to their own first synthetic opioid death (Table 7, Panel A). The spillover ATTs are small and statistically indistinguishable from zero under the first-occurrence and sustained-entry definitions, though the acute-escalation estimate is significant (5.64, SE = 2.17, $p < 0.01$) a point we return to below since acute escalation is also the definition most sensitive to regional co-movement. On balance, the spillover ATTs remain far smaller than the main-sample estimates (Table 4), suggesting that the prescribing response is triggered primarily by local mortality, not regional awareness of neighboring mortality shocks.

Restricting the comparison group to non-adjacent not-yet-treated counties produces consistently positive and significant ATTs (Panel B). Under the first occurrence shock definition the estimate is 18.52 patients per 100,000 (SE = 2.83, $p < 0.001$), and estimates are similar across all three shock definitions. These estimates are somewhat larger than the main results, which is expected when border counties are removed from the comparison group. Geographic

spillovers are not driving the positive main estimates and, if anything, their presence in the main comparison group modestly attenuates our results.

6.4 Heterogeneity

We examine heterogeneity by: (i) rural vs. urban counties (RUCC 1–3 = metro, 4–9 = nonmetro), (ii) payer, (iii) provider specialty, (iv) baseline overdose burden (above/below median), and (v) pre-existing buprenorphine prescribing (above/below median).

Figure 3 and Table A8 presents heterogeneity in treatment effects for each measure. For both the first occurrence (FO) and acute escalation (AE) shocks, the response is concentrated in non-metropolitan counties (FO: ATT = 21.11, SE = 3.44; AE: ATT = 9.97, SE = 3.58), with no significant effect in metropolitan counties (FO: ATT = 2.84, SE = 3.81; AE: ATT = 0.22, SE = 2.29). The sustained entry (ST) measure finds little difference in response between urbanicity levels (metro: ATT = 22.81, SE = 3.58; non-metro: ATT = 22.51, SE = 3.99). By payer, Medicaid prescriptions drive the bulk of the response across specifications (FO: ATT = 9.36, SE = 2.04; AE: ATT = 3.64, SE = 1.30; ST: ATT = 14.48, SE = 2.17), with smaller or insignificant effects for other payers. This concentration among Medicaid patients is corroborated by two related findings on the ACA Medicaid expansion in Section 6.7: the baseline ATT is robust to directly controlling for state Medicaid-expansion status, and the response is significantly larger in states that had already expanded Medicaid at the time of treatment, consistent with evidence that ACA Medicaid expansion increased buprenorphine prescribing [Siegal et al., 2026, Meinhofer and Witman, 2018]. Among provider specialties, advanced practice providers (APP) show the largest response (FO: ATT = 9.15, SE = 1.78; AE: ATT = 6.12, SE = 1.58; ST: ATT = 16.08, SE = 2.37), followed by psychiatry (FO: ATT = 2.28, SE = 0.65; AE: ATT = 1.28, SE = 0.52; ST: ATT = 1.65, SE = 0.65). Notably, only the sustained entry measure has an impact on primary care prescribing (ATT = 8.01, SE = 1.65). The Medicaid and APP concentration is consistent with these provider types serving as front-line responders to the crisis in underserved areas. The response is also larger

in counties with above-median baseline overdose burden (FO: 19.49 vs. 7.15; AE: 9.89 vs. 1.16, n.s.; ST: 29.90 vs. 19.34) and above-median baseline buprenorphine prescribing (FO: 22.35 vs. 1.92, n.s.; AE: 18.18 vs. -6.27; ST: 34.07 vs. 14.07), suggesting that the prescribing response builds on existing treatment infrastructure.

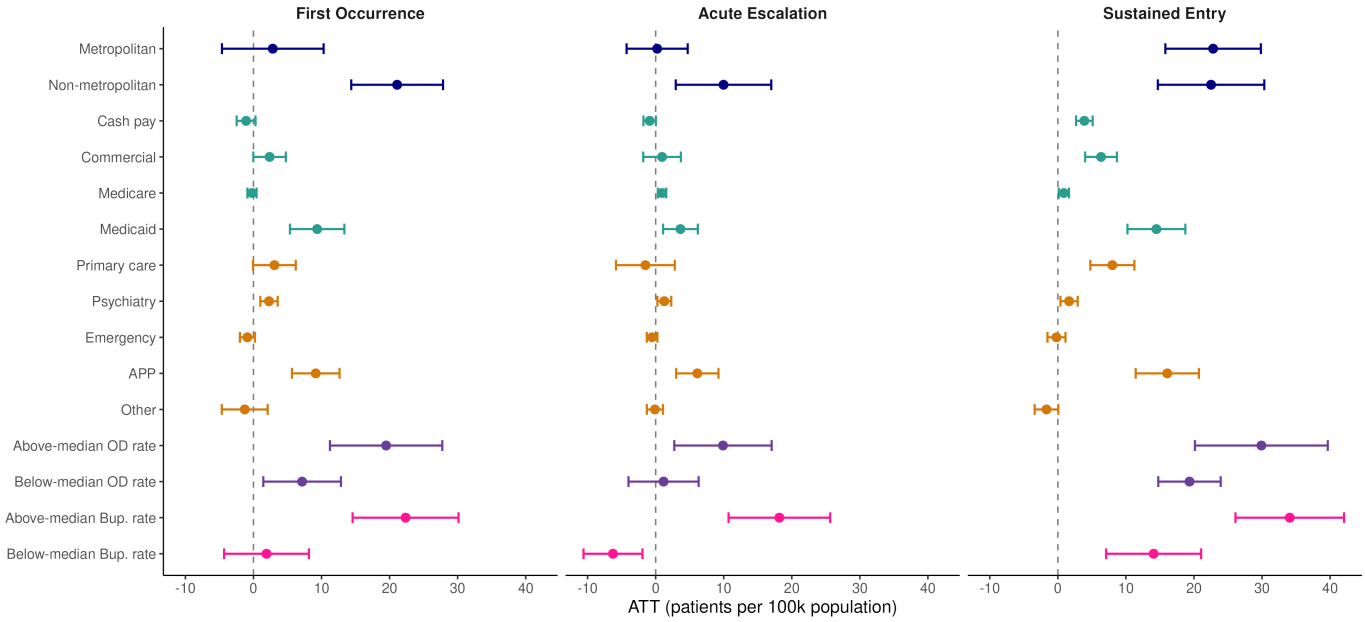


Figure 3: Heterogeneity in Treatment Effects Across Shock measures

6.5 Treatment Effects by Cohort Era

We decompose the overall ATT by treatment cohort era to examine whether effects vary across the sample period and to assess robustness to excluding late-pandemic cohorts, where the comparison set is thinnest. Figure 4 presents ATTs for two cohort groups of counties first experiencing a synthetic opioid shock in 2013–2019 and 2020–2022, alongside both the pooled estimate and the estimate excluding 2023 when the X waiver was removed, separately for each shock definition.

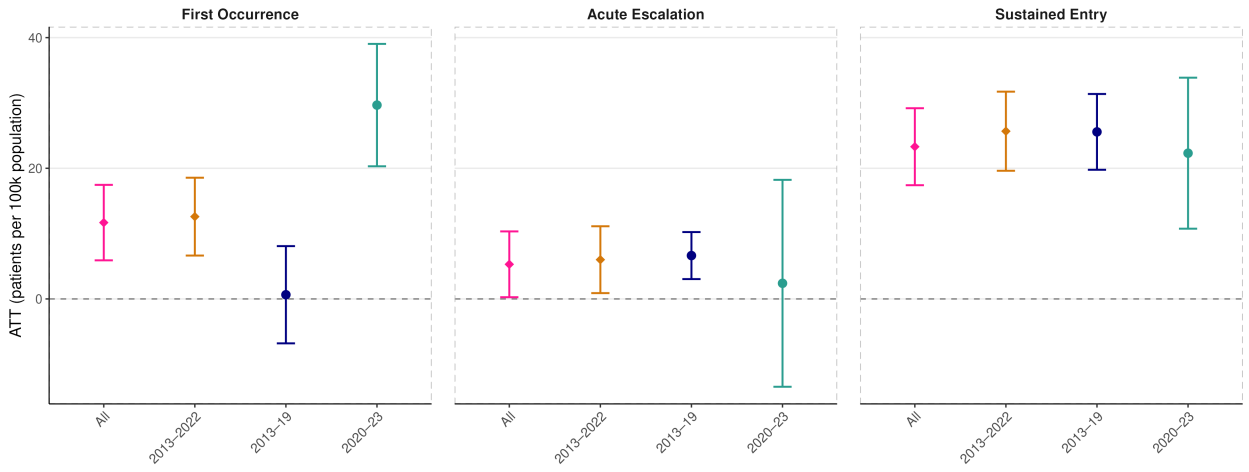


Figure 4: Effects over sample period by shock

For the first-occurrence measure, the overall ATT is driven primarily by post-2020 cohorts. This concentration coincides with the COVID-19 era expansion of telehealth prescribing and the 2023 elimination of the X-waiver requirement. For counties crossing the first-occurrence threshold after 2020, we interpret this as an enabling effect that highlights once regulatory barriers to buprenorphine prescribing diminished, providers were better positioned to respond to mortality shocks, amplifying the behavioral response we document. The X-waiver robustness check (dropping 2023 cohorts) leaves estimates nearly identical (12.6 vs. 11.7), which suggests our estimates are not driven by the X-waiver elimination specifically but does not address the broader telehealth and COVID-era regulatory changes.

The acute-escalation measure shows the opposite pattern with the pre-2020 estimate being significant while the post-2020 estimate is not, likely reflecting reduced power as the comparison pool shrinks after 2020. The sustained-entry measure produces significant estimates in both periods, making it the most robust to this concern. The acute-escalation and sustained-entry measures are less exposed to this concern, since they yield significant estimates precisely in the pre-2020 period before major regulatory disruptions of the pandemic era. The first-occurrence result should be interpreted with caution given its post-2020 concentration.

As a further check, we assess whether the elimination of the X-waiver requirement in

January 2023 drives our findings by re-estimating on cohorts first treated in 2013–2022 only, dropping counties whose first shock falls in 2023. The ATTs are 12.6 (SE = 3.0), 6.0 (SE = 2.6), and 25.7 (SE = 3.1) patients per 100,000 under the first-occurrence, acute escalation, and sustained-entry definitions, respectively. These are nearly identical to the full-sample estimates of 11.7, 5.3, and 23.3, indicating that the X-waiver removal is unlikely to account for our results.

6.6 Targeted Analysis of the Synthetic Opioid Response Population

The primary outcome captures the overall prescribing response but cannot distinguish whether providers are treating a new synthetic opioid-exposed population or expanding treatment for patients with prior prescription opioid or heroin use disorder. Two features of synthetic opioid use disorder allow us to identify prescribing more specifically directed at the synthetic opioid population.

First, effective treatment of synthetic opioid use disorder may require higher buprenorphine doses than those historically used for prescription opioid or heroin addiction [Chambers et al., 2023, Nunes et al., 2024, Shiwach et al., 2025]. If the prescribing response reflects adaptation to the synthetic opioid population, we would expect it to manifest not only in more patients but in higher average doses per patient. We examine the FDA recommended target dose of 16mg and upper limit of 24mg as thresholds for buprenorphine maintenance treatment. Chambers et al. [2023] document that a majority of patients dosed at even these levels discontinued treatment within 180 days during the fentanyl era, and that some fentanyl-exposed patients require doses above the FDA-approved ceiling, up to 32mg based on prior observational evidence. An increase in the share of patients exceeding these thresholds therefore indicates prescribing beyond the pre-fentanyl clinical standard, consistent with providers adapting to a population that requires higher doses to remain in treatment. Second, the synthetic opioid population skews younger and includes individuals without prior treatment contact, unlike prior crisis populations [Tanz et al., 2022, Friedman et al., 2022].

We examine four dosing outcomes: average daily buprenorphine dose per patient in the county (in mg and in MME), and the share of buprenorphine patients whose dose exceeds 16mg or 24mg per day. Section 3.1.1 details the construction of these measures, including how daily dose is inferred from IQVIA strength and quantity fields for both sublingual and extended-release injectable formulations.

The evidence on this margin is mixed rather than uniform: no dosing outcome moves significantly and in the same direction across all three shock definitions, average dose rises only under acute escalation, and the most consistent signal is a small, recurring increase in the share of patients exceeding the 24mg ceiling under two of the three definitions. We discuss below why this bounded pattern is itself informative, rather than treating it as a failure to detect an effect.

Table 8: Targeted Outcomes: Dosing

	(1)	(2)	(3)	(4)
	Avg. Daily Dose (mg)	Avg. Daily Dose (MME)	Share >16mg/day	Share >24mg/day
Panel A: First occurrence				
ATT	-0.012	-0.352	-0.001	0.004*
	(0.051)	(1.531)	(0.003)	(0.002)
Pre-treatment mean	13.96	418.85	0.28	0.04
Percent effect	-0.08%	-0.08%	-0.32%	8.37%
Panel B: Acute escalation				
ATT	0.107*	3.203*	-0.006*	0.001
	(0.05)	(1.493)	(0.003)	(0.002)
Pre-treatment mean	13.88	416.31	0.28	0.05
Percent effect	0.77%	0.77%	-2.09%	2.25%
Panel C: Sustained entry				
ATT	0.048	1.431	0.003	0.003**
	(0.047)	(1.402)	(0.003)	(0.001)
Pre-treatment mean	14.05	421.43	0.27	0.04
Percent effect	0.34%	0.34%	1.04%	7.32%

Notes: Estimator: Callaway–Sant'Anna (2021), doubly robust, matched county-quarter panel, 5,000 bootstrap iterations, county-clustered SEs. Share thresholds (16mg, 24mg) correspond to the FDA-recommended target dose and FDA-approved upper limit for buprenorphine maintenance treatment, respectively. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

The dosing evidence is mixed, not uniform across outcomes and shock definitions. Average daily dose rises significantly under acute escalation (+0.107mg and +3.20 MME, both $p < 0.05$), a 0.8 percent increase relative to the pre-treatment mean on each measure, but is not significantly different from zero under first occurrence or sustained entry. The share of patients exceeding 24mg per day (the FDA-approved upper limit) rises significantly under first occurrence and sustained entry (+0.004 and +0.003 percentage points, respectively), an 8.4 percent and 7.3 percent increase relative to each definition's own pre-treatment share;

expressed this way, the movement across the 24mg ceiling is proportionally larger than the percentage-point changes alone suggest, even though it remains a minority of patients. We do not find a single outcome that increases significantly and consistently across all three shock definitions; the most consistent signal, in both statistical and relative-magnitude terms, is this rise in patients crossing the 24mg ceiling, present under two of the three measures. The one definition under which average dosing rises is acute escalation, the aberration-based measure that most directly captures a mortality surprise relative to a county's own recent baseline. This is also the definition under which new provider entry, and not expansion of existing panels, drives the patient-count response (Table 5), so there is less new-patient dilution of the county average than under the other two definitions. The accompanying decline in the share above 16mg (a 2.1 percent relative decrease) indicates that this movement occurs within the conventional maintenance range without being in the upper tail, consistent with modest upward standardization of dosing among the existing patient stock, not escalation past the labeled thresholds. Given the magnitude and the number of estimates in this table family, we treat this pattern as suggestive. Features of the setting imply that muted average-dose effects are consistent with, and even predicted by, the patient-count response. The average-dose outcome is computed over a patient mix that treatment itself changes, as newly inducted patients begin at 2–4mg with titration over subsequent days, so an inflow of new patients mechanically dilutes the county-average dose even if continuing patients' doses rise. The dilution should be largest under acute escalation, where new provider entry drives the response (Table 5), and this is where the share above 16mg declines. The dose margin was administratively constrained during the sample period for the payer segment driving our response when most state Medicaid programs imposed quantity or dose limits on buprenorphine, and prior authorization requirements targeted at doses above 16mg have been shown to reduce high-dose use [Clark et al., 2014]. Providers responding to a mortality shock could expand freely on the patient-count margin while the dose margin required administrative effort, which makes the recurring increase in the share crossing the 24mg ceiling the more

informative signal. The clinical consensus that fentanyl-exposed patients benefit from higher doses consolidated late in our sample period [Chambers et al., 2023, Nunes et al., 2024], after most treatment cohorts crossed their shock thresholds, so contemporaneous dose adaptation would be surprising.

Taken together, we read the dosing evidence as suggestive. No dosing outcomes are significantly affected or in the same direction across all three shock definitions. The estimates that are significant are small: the acute escalation average-dose effect is roughly a tenth of a milligram, and the increases in the share crossing 24mg are fractions of a percentage point. With four outcomes and three shock definitions, some scattered significance is expected by chance. Several measurement features also work against detection: the depot-injectable dose conversion is approximate (though the sublingual-only results in Table A11, Appendix Section G, rule it out as the driver), and county-quarter averaging compresses within-county dose variation. What the evidence does support is a bounded conclusion. The response to local mortality shocks operates on the patient-count margin. There is no detectable dose escalation among established patients, and the only recurring dose signal is a small movement across the 24mg line under two of three definitions. That bounded pattern is itself informative about which margins were available to responding providers during this period. Prescribing above 24mg was a niche practice, accounting for roughly 2 percent of dispensed buprenorphine prescriptions in 2019 and 2020, with over 80 percent of such prescriptions written by 4 percent of prescribers, and it was rarely covered by Medicaid, the payer segment driving our patient-count response [Stein et al., 2025]. It also required a decision against labeling language that insurers and some state programs operationalized as a ceiling [Grande et al., 2023, Clark et al., 2014]. Against that friction, a broad dose response would have been surprising, and the small movement we detect at the 24mg line stands in contrast to the absence of any positive cross-sectional association between state fentanyl mortality and high-dose prescribing in the same era [Stein et al., 2025]. We therefore interpret the dosing results as consistent with, but not by themselves establishing, adaptation

to the synthetic opioid population, and we regard the question of whether providers escalate doses in response to local mortality, particularly across payer segments facing different dose restrictions, as a priority for subsequent work.

We separately examine the age composition of the treated population, grouping patients into three non-overlapping bands: 18–29, 30–64, and 65+, and expressing each outcome per 100,000 population of the corresponding band. Figure 5 presents the age-composition outcome for each band. The largest and most consistent increases occur among patients aged 30–64 (first occurrence: 25.3 additional patients per 100,000 of that age band, $p < 0.001$; sustained entry: 43.6, $p < 0.001$). Patients 18–29 also increase significantly under acute escalation (11.5, $p < 0.05$) and sustained entry (24.7, $p < 0.001$). Patients 65 and older show no significant response under any shock definition. The response is therefore concentrated in the working-age population broadly.

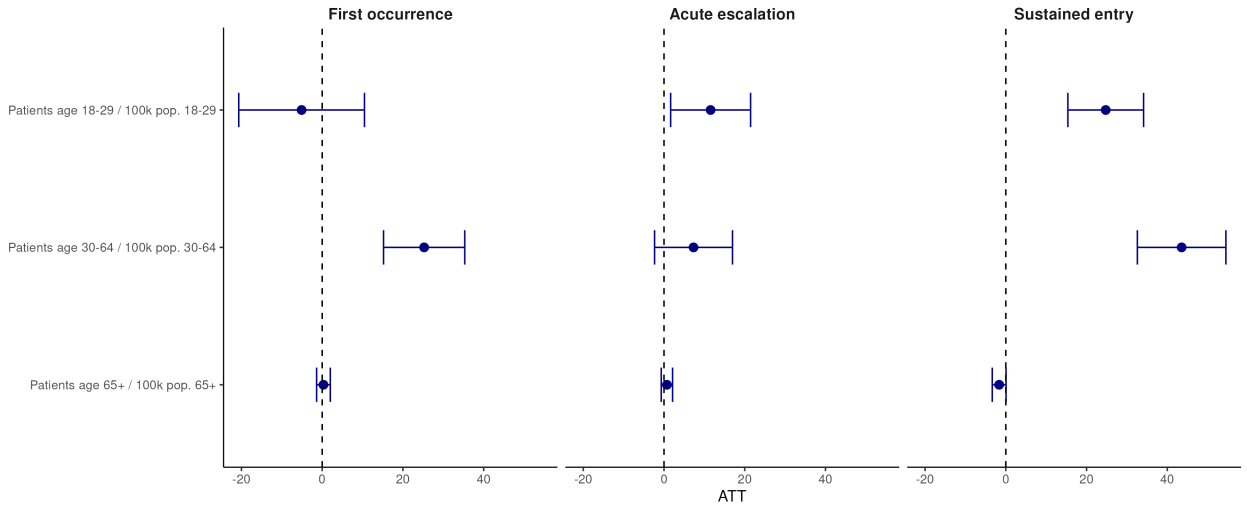


Figure 5: Age Composition of Buprenorphine Patients: ATT by Shock Definition

Decedent-Age Composition of the Mortality Signal

We next estimate the county-quarter breakdown of synthetic opioid deaths by decedent age (under 30, 30–50, 51–64, and 65 and older). We construct two complementary tests, both using the identical matching and estimation specification as the main analysis. First, we

redefine each of the three shock-timing variables using only deaths within a single decedent-age bin and compare the resulting ATT to the all-ages estimate. Second, we split treated counties by whether the share of their pre-onset synthetic opioid deaths involving decedents under 30 is above or below the sample median, and re-estimate the main (all-ages) shock ATT within each subgroup.

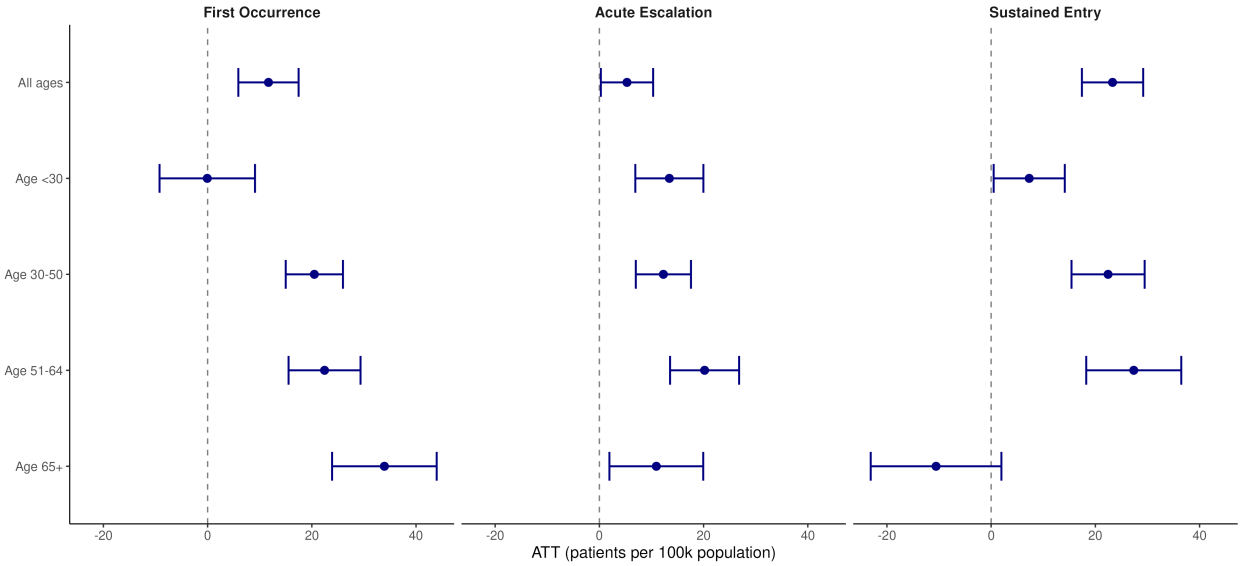


Figure 6: ATT by Decedent Age Bin Defining the Shock

Figure 6 presents the age-restricted shock results. The results do not support the hypothesis that younger decedent age drives a larger provider response. Under first occurrence, shocks restricted to decedents under 30 produce a null estimate, while shocks restricted to decedents aged 30–50 and 51–64 produce large, significant effects that meet or exceed the all-ages estimate (11.68). The pattern holds under acute escalation, where the under-30 estimate is smaller than the 51–64 estimate, and under sustained entry, where the under-30 estimate is the smallest of the four age bins and the 65-and-older estimate turns negative and insignificant. This last cell is estimated on a substantially smaller treated sample than the other three age bins, given how comparatively rare synthetic opioid deaths among decedents 65 and older remain, and should be interpreted with caution. Across all three shock definitions, the 51–64 bin produces the largest or second-largest estimate, and effects are con-

sistently stronger for shocks restricted to decedents aged 30 and older than for the under-30 bin.

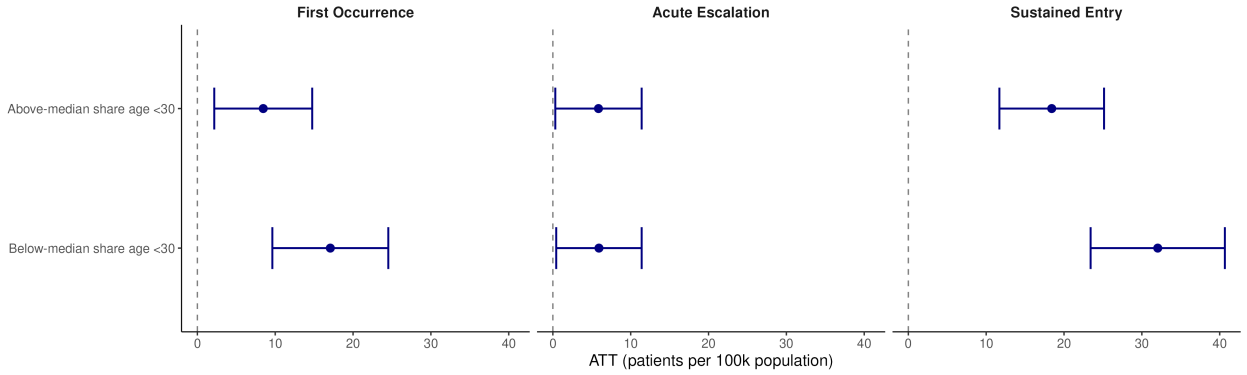


Figure 7: Heterogeneity in the Main Shock ATT by Decedent-Age Composition

Figure 7 presents results using age as a moderator, which reinforce this pattern. Counties where a below-median share of pre-onset deaths involved decedents under 30 show a larger main-shock response than counties with an above-median young share, under both first occurrence (17.08 vs. 8.46) and sustained entry (32.04 vs. 18.42); the difference is negligible under acute escalation (5.92 vs. 5.86).

These results suggest that the operative signal is deaths that resemble a population a provider might recognize as plausible OUD treatment candidates, being working-age adults in the 30–64 range. These deaths are also more legible as avoidable, given that a working-age adult with an established pattern of opioid use who dies of a synthetic opioid overdose represents an outcome a provider might plausibly have forestalled with treatment, whereas a death from a single counterfeit-pill exposure among a decedent with no prior treatment contact offers no comparable signal of a treatable local population. This is consistent with the CDC finding cited in Section 2.3 that many adolescent and young-adult synthetic opioid decedents lack a documented history of opioid use or treatment contact [Tanz et al., 2022, Friedman et al., 2022]. Such deaths, while potentially more alarming to the broader community, may be less legible to a provider as evidence of an existing, treatable local OUD population than deaths among working-age adults who more closely resemble the patients

providers already see or could plausibly expect to treat. We note that this decedent-age result characterizes the age distribution of the decedents driving the mortality shock, which is conceptually distinct from the age distribution of the patients who subsequently receive buprenorphine (Figure 5). The mortality data do not link individual decedents to subsequent treatment, so we cannot directly test whether the same working-age adults drive both patterns. The decedent-age pattern is also consistent with a patient-demand channel operating along with provider salience, as deaths among working-age adults with established opioid use indicate a surviving local population with treatable OUD who may present for care. A death within an established local drug-using network is plausibly most salient to the peers who shared that network and who may themselves have an undiagnosed or untreated OUD, so the same working-age deaths that make a county's OUD population most legible to providers may also be the deaths most likely to prompt care-seeking among the surviving users who knew the decedent. Deaths from one-time counterfeit-pill exposure among young decedents, by contrast, indicate no comparable latent treatment demand. The reduced form captures both provider updating as well as the presentation decisions of surviving users, and both channels predict the observed concentration of effects in the 30–64 range.

6.7 State Policy Environment

A concern raised in Section 4.2 is that state policy changes correlated with synthetic opioid entry timing could confound our estimates. We first estimate specifications that directly control for state-level policies as time-varying covariates. Then, we examine heterogeneity in treatment effects by the policy environment at the time of treatment, which provides evidence on how policies interact with the organic behavioral channel we document. We consider nine policy and covariate dimensions: (i) Good Samaritan laws removing arrest risk for overdose reporters, (ii) naloxone access laws with standing orders or third-party prescribing authority, (iii) must-access prescription drug monitoring program (PDMP) requirements for opioids, (iv) Medicaid expansion under the ACA, (v) marijuana legalization (entered as two

separate covariates, medical legalization and the start of recreational retail sales), (vi) nurse practitioner full practice authority, removing the requirement for a written collaborative or supervisory agreement with a physician, which governs whether NPs can prescribe buprenorphine independently [Spetz et al., 2019], (vii) triplicate prescription program states, (viii) 1996 county-level cancer mortality, following the pre-OxyContin marketing-exposure design in Arteaga and Barone [2026], and (ix) county location east versus west of the Mississippi River as a proxy for early versus late synthetic opioid market penetration [Ciccarone, 2019, Bryce Pardo et al., 2019, Donahoe and Soliman, 2025].

Figure 8 re-estimates the overall ATT controlling for each of seven time-varying policy dimensions in turn, and for all seven together, alongside the uncontrolled baseline specification.

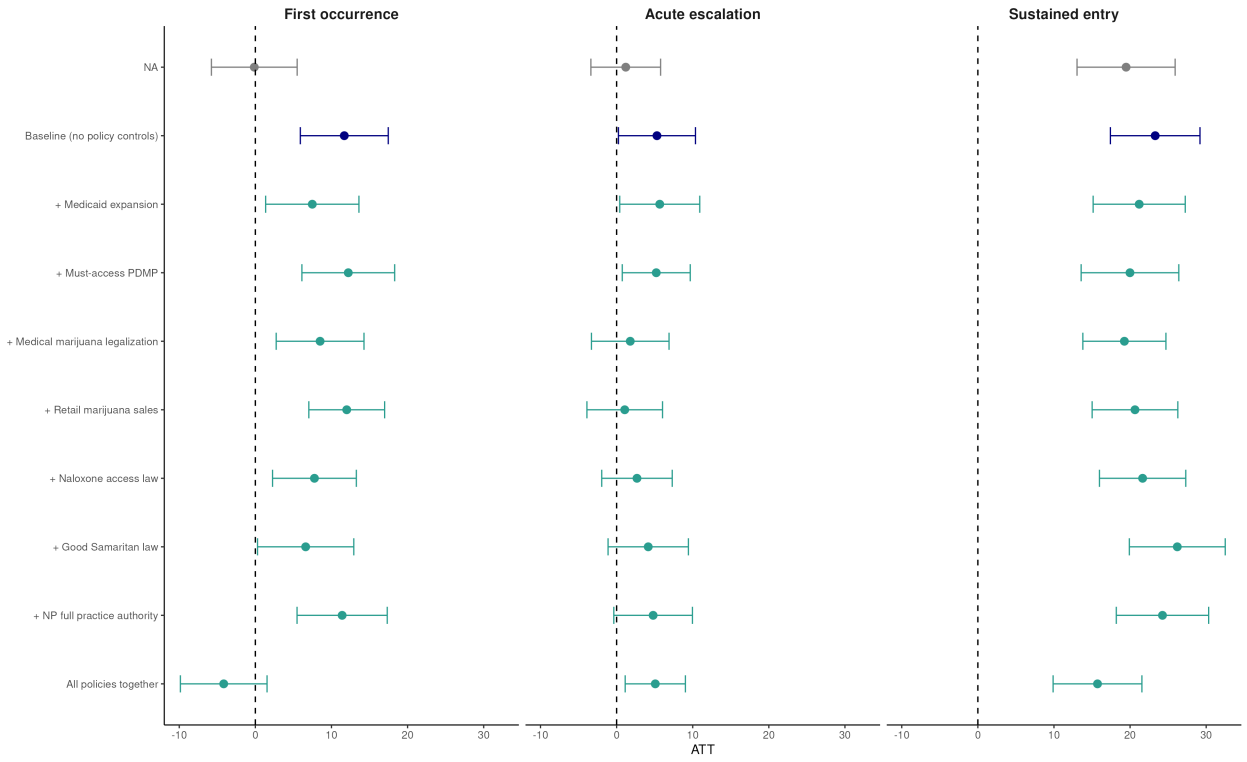


Figure 8: Main ATT Under Alternative Policy Controls

Under first occurrence and sustained entry, the baseline ATT is robust to controlling individually for each of state Medicaid expansion, must-access PDMP, medical marijuana

legalization, retail recreational marijuana sales, naloxone access, Good Samaritan, and NP full-practice-authority laws, with point estimates remaining statistically significant throughout. Under acute escalation, whose baseline estimate is itself only marginally significant (5.30, $p < 0.05$), several individual controls (medical marijuana legalization, retail recreational sales, naloxone access, Good Samaritan, and NP full-practice authority) bring the ATT below conventional significance, though the point estimate remains positive in every case. When all seven policy controls are included simultaneously, the ATT becomes insignificant for first occurrence (-4.16) but remains significant for acute escalation (5.08, $p < 0.05$) and sustained entry (15.72, $p < 0.001$). We interpret the fully-saturated specification with caution for two reasons. First, including seven correlated state-policy indicators together reduces power considerably. Second, the Callaway–Sant'Anna framework conditions on covariates measured before treatment, and Caetano et al. [2026] show specifications with time-varying covariates are not robust when those covariates are themselves affected by the treatment; several of these policies (naloxone access, Good Samaritan, must-access PDMP) are legislative responses to the same crisis that defines our treatment, so controlling for their post-treatment values conditions on a mediator. Caetano et al. [2026] show how that dropping such covariates entirely is also ill-advised, and derive conditions under which conditioning on their pre-treatment values recovers the parameter of interest, which leads naturally to the Callaway–Sant'Anna estimator with pre-treatment covariate values. They extend these results to staggered adoption. For this reason, our preferred evidence on policy confounding is the heterogeneity analysis below, which evaluates each policy at its pre-determined status in the county's treatment quarter.

We separately examine heterogeneity in treatment effects across all nine policy and covariate dimensions, splitting treated counties into those with vs. without the policy or characteristic in effect. For the six time-varying policies, effect status is evaluated at each county's own treatment quarter and not a fixed calendar date, so counties treated at different points in the sample are each compared against their own contemporaneous policy environment.

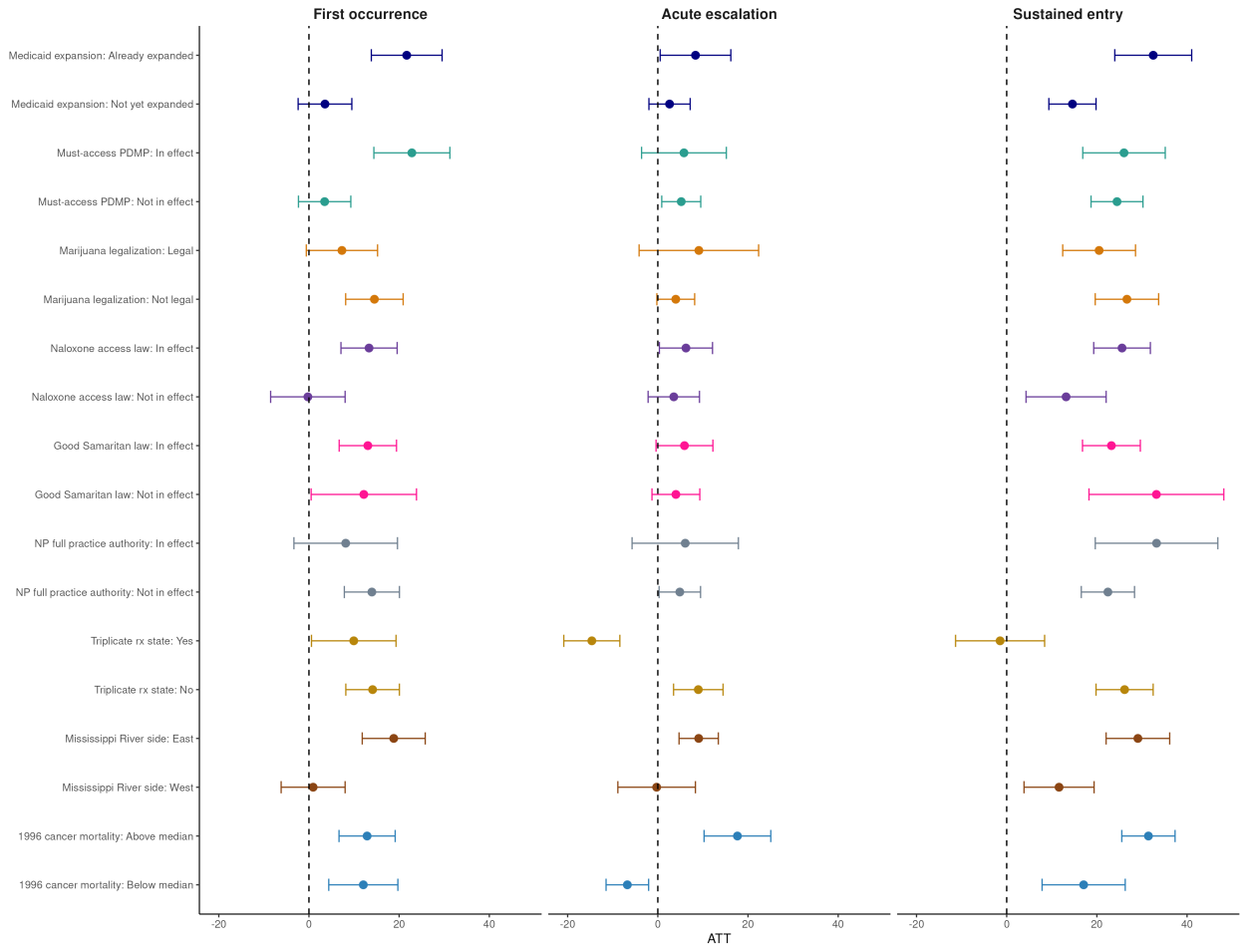


Figure 9: Heterogeneity by Policy/Covariate Environment at Treatment

Most stratifications show little difference between counties in either group, indicating broad effects for our results, regardless of policy status. We do note three patterns which are consistent across all three shock definitions. First, the response is systematically larger in counties east of the Mississippi River than west (sustained entry: 29.10 vs. 11.61, both significant), consistent with the east/west market-penetration hypothesis motivating this covariate. Second, the response is concentrated in states that had already expanded Medicaid at the time of treatment (sustained entry: 32.50 vs. 14.58), consistent with prior studies linking Medicaid expansion to access for MOUD [Siegal et al., 2026, Meinhofer and Witman, 2018]. Third, counties in triplicate-prescription-program states show a systematically weaker response relative to non-triplicate states (acute escalation: -14.64 vs. 8.98; sustained entry:

-1.46, not significant, vs. 26.15).

6.8 Placebo Test: Other Mortality Shocks

If the response is specific to synthetic opioid-related mortality, sudden rises in unrelated deaths should not produce similar effects on buprenorphine prescribing. We construct analogous shock measures using nine alternative causes of death: cocaine deaths (ICD-10 T40.5), alcohol poisoning (ICD-10 T51.0–T51.4), vehicle deaths (ICD-10 V01–V99; NCHS 113-cause recode category 114), suicide (ICD-10 X61–X63, X65–X84, Y87.0), influenza (ICD-10 J10–J11), chronic liver disease (ICD-10 K70, K73–K74), kidney disease (ICD-10 N00–N07, N17–N19, N25–N27), diabetes mellitus (ICD-10 E10–E14), and Alzheimer's disease (ICD-10 G30). The suicide definition excludes ICD-10 X60 and X64, which fall within the conventional X60–X84 suicide range but reflect drug poisoning already captured by our synthetic opioid and other overdose measures. The cocaine and alcohol placebos are similarly restricted to deaths with no co-occurring narcotic, sedative, psychotropic, or other-drug involvement recorded on the death certificate, so that, to the best of our ability given multiple-cause-of-death coding, these placebos are not themselves contaminated by synthetic opioid co-involvement. These causes span drug-adjacent, behavioral, infectious, and purely metabolic or degenerative etiologies, providing a stringent test of specificity.

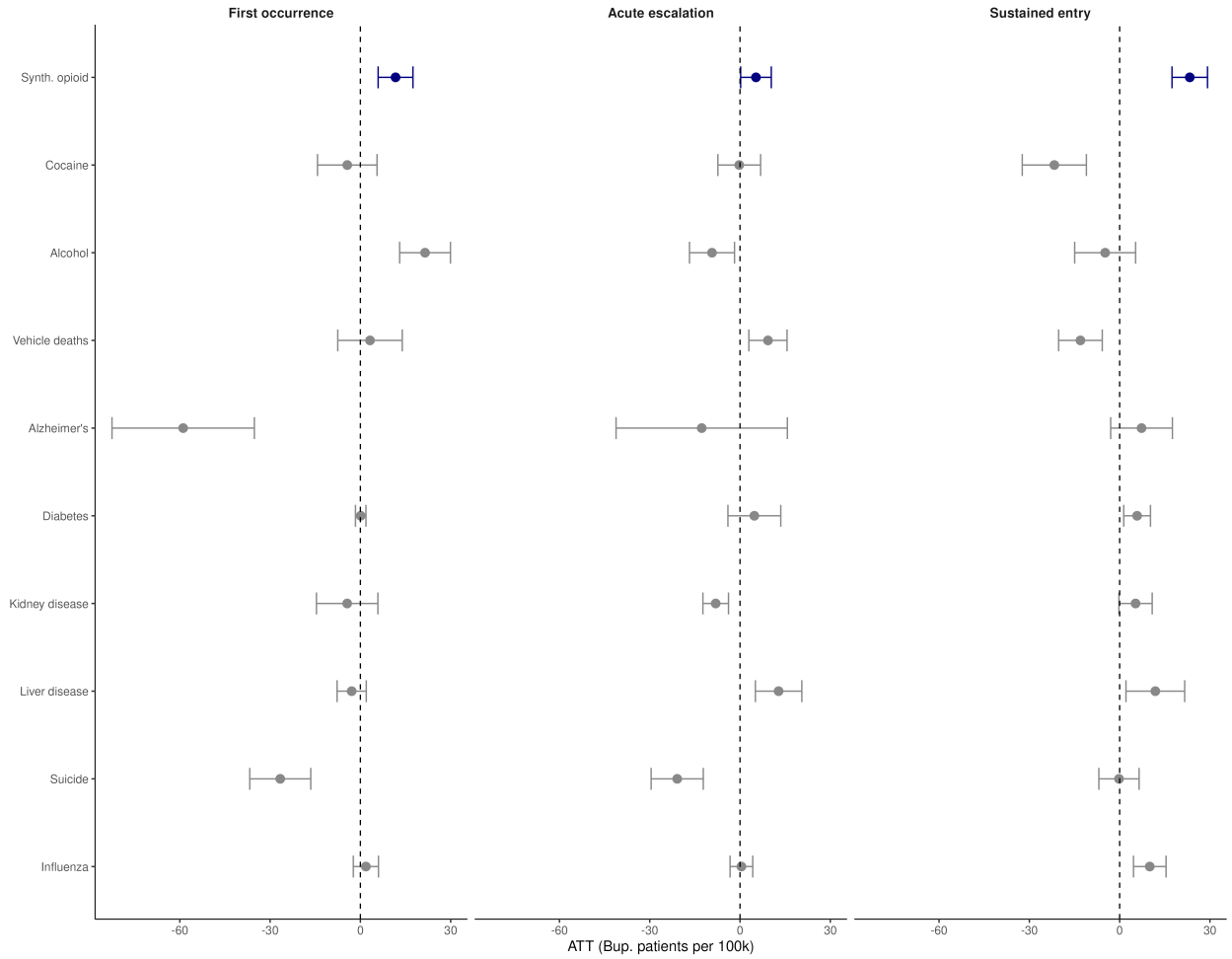


Figure 10: Placebo Mortality shocks

Figure 10 presents the results. Across all three shock definitions, synthetic opioid shocks produce large, positive, and statistically significant increases in buprenorphine prescribing. None of the nine placebo series replicates this pattern. Cocaine and alcohol poisoning, the two placebos closest to our setting in involving substance use directly, behave like the main specification-sensitivity checks elsewhere in this paper: individual estimates are occasionally significant, but the sign and significance are not consistent across all three shock definitions as for the synthetic opioid result. Vehicle deaths show the same pattern, positive for the first-occurrence and acute-escalation definitions but turning negative and significant under sustained entry. The remaining causes, spanning suicide, influenza, liver disease, kidney disease, diabetes, and Alzheimer's disease, share no biological or policy link to opioid use

disorder and likewise fail to reproduce the positive, significant, and consistent pattern of the synthetic opioid shocks across all three definitions; where an individual coefficient is significant, it is not accompanied by significant, same-signed estimates under the other two shock definitions, unlike our main result. Taken together, the placebo evidence is consistent with a prescribing response that is specific to the synthetic opioid entry: no alternative cause of death, including two restricted to exclude co-occurring drug involvement, reproduces the full pattern that defines our main result.

We note that placebo samples are considerably smaller than the synthetic opioid sample, particularly for cocaine under the sustained-entry definition (273 treated counties), because the study period (2013–2023) was defined by the synthetic opioid wave. Cocaine and vehicle deaths exhibited far fewer county-level spikes during this era, reducing power. The non-drug causes are more common but also more uniformly distributed across counties and time, leaving fewer counties untreated to serve as controls.

6.9 Sensitivity to Shock Definition

A central feature of our design is the construction of the treatment indicator: which quarter a county first crosses a given synthetic opioid mortality threshold. We examine 25 alternative shock definitions spanning five conceptual families: (i) raw death count thresholds (>0 through >5 synthetic opioid deaths in a quarter), (ii) SD-based escalation relative to a four-quarter rolling average (0.50 to 2.00 SDs above the local mean), (iii) consecutive quarters with any synthetic opioid death (one through four), (iv) analogous count and SD thresholds applied to any opioid deaths, (v) analogous thresholds applied to all drug overdose deaths, and (vi) rate-based thresholds applied to synthetic opioid deaths per 100,000. For each definition we re-estimate the full matched CS-DiD pipeline and aggregate to a single post-treatment ATT.

Figure 11 presents the results as a grouped forest plot. All 25 specifications yield positive ATT estimates, and 20 of 25 are statistically significant at the 5 percent level. The

five exceptions are the broader any-opioid and any-drug specifications at the >1-death and 3-consecutive-quarter thresholds, along with the rate-based 1-SD-escalation specification, which likely capture transient or marginal mortality events that generate weaker salience. The direction of the effect is therefore robust across every conceptualization of a synthetic opioid shock we consider. Magnitudes increase with threshold stringency within each family, consistent with a dose-response pattern in which more severe shocks elicit larger prescribing responses. However, the three main specifications (highlighted in navy) sit in the lower-middle range of estimates, indicating they are conservative. Results are considerably weaker and more heterogeneous for the all-drug overdose estimates. The acute escalation for any-drug specification yields a significant positive ATT (7.9 patients per 100,000, $p < 0.001$), but the first occurrence and sustained entry variants are statistically indistinguishable from zero. This pattern suggests that it is specifically the synthetic opioid mortality signal, not simply a general rise in drug overdose deaths, that drives provider prescribing responses, consistent with the salience of the synthetic opioid crisis as a distinct policy-visible event.

Our three main specifications were selected to balance sample coverage against threshold meaningfulness. Within the count threshold family, the >1 death definition maximizes treated county coverage (1,654 counties). Stricter thresholds progressively exclude counties that never experience high-count mortality events, falling to 982 treated counties at >5 deaths, while the >0 threshold loses counties to pre-period data constraints from early-affected counties treated in the first sample quarters. The same pattern holds for SD-based escalation. The 1.00-SD threshold sits at the sample-size peak (1,968 treated counties), with both lower and higher cutoffs shedding counties. For consecutive quarters, the three-quarter requirement (1,578 counties) balances the need to distinguish sustained crises from transient single-quarter spikes while retaining more counties than the four-quarter definition (1,470). The main specifications therefore represent neither the loosest nor the strictest possible definitions but rather the point within each family where power and interpretability are jointly maximized.

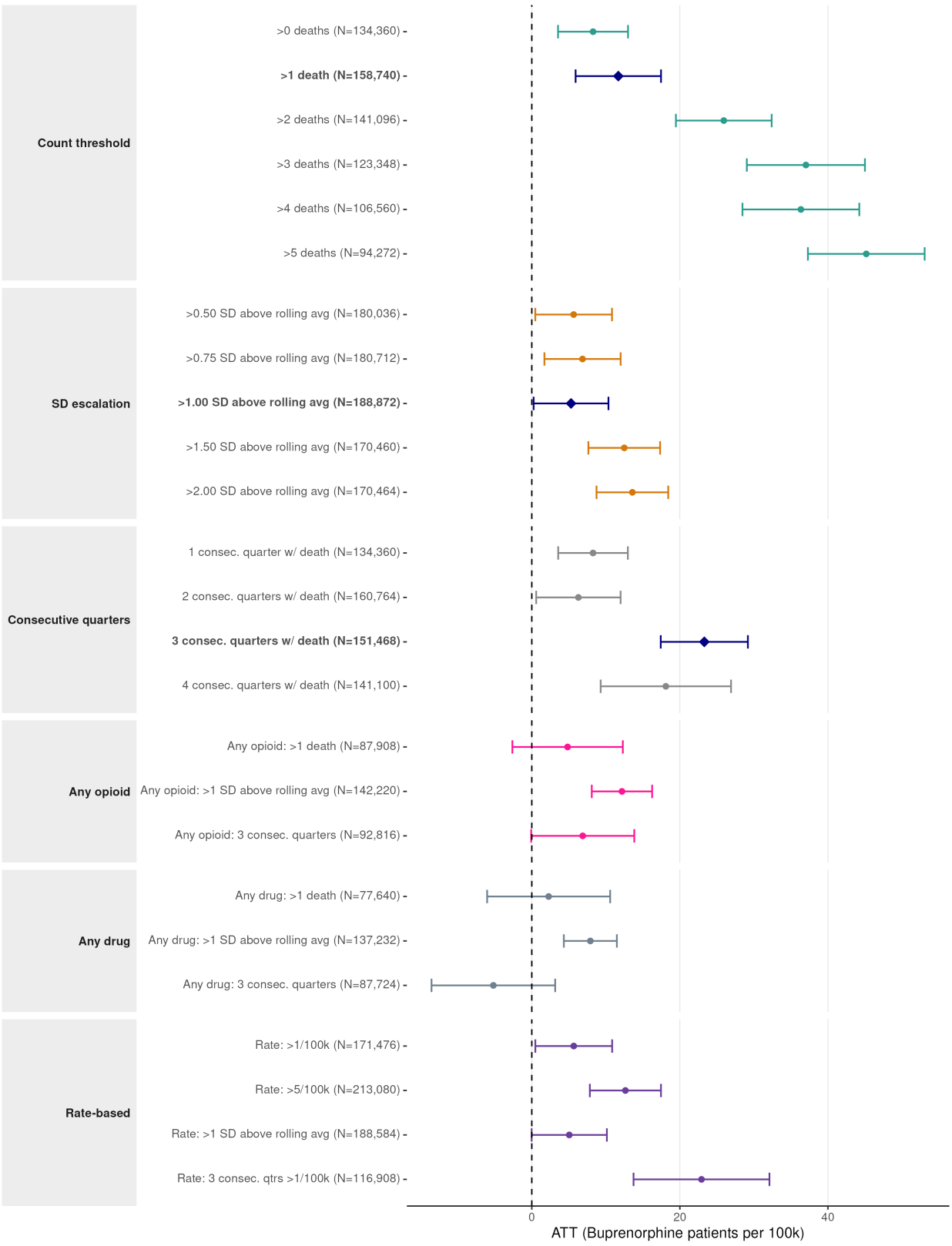


Figure 11: Sensitivity of ATT Estimates to Shock Definition

Notes: Each row shows the overall post-treatment ATT ± 95% CI from the matched CS-DiD pipeline. Diamond markers indicate the three main specifications. Color identifies the specification family; navy highlights main specifications within their group.

6.10 Information Salience

A prerequisite for information salience is that deaths are informative about the underlying level of synthetic opioid presence in local drug markets. A concern with mortality-based shock measures is that deaths are a lagging indicator, may be suppressed in sparse counties, or may diverge from other measures of fentanyl exposure. We assess this by comparing county-level synthetic opioid mortality to two alternative measures of fentanyl presence: drug seizure reports from the National Forensic Laboratory Information System (NFLIS) and opioid-related hospital encounters from the Healthcare Cost and Utilization Project (HCUP) Fast Stats.

Figure 12 presents state-year scatter plots of synthetic opioid mortality rates against NFLIS fentanyl drug reports per 100,000 population ($r = 0.692$, $p < 0.001$), opioid inpatient stays per 100,000 ($r = 0.490$, $p < 0.001$), and opioid emergency department visits per 100,000 ($r = 0.613$, $p < 0.001$). Across all three comparisons, mortality tracks closely with independent measures of synthetic opioid exposure, validating its use as a signal of underlying community opioid burden.[4]

[4]NFLIS collects drug chemistry reports from federal, state, and local forensic laboratories; HCUP Fast Stats reports hospitalization rates from the NIS and NEDS samples. Both are independent of NVSS mortality data. Several limitations apply. First, NFLIS coverage is incomplete: not all forensic laboratories participate, and drug report counts reflect both the availability of fentanyl in the local drug supply and the intensity of law enforcement seizure activity, which may vary across states and years independent of actual supply. Second, HCUP state participation is voluntary and uneven; roughly a third of states are missing in any given year, so the correlation is estimated on an unrepresentative subset of states with above-average hospital reporting infrastructure. Third, and most importantly, both NFLIS and HCUP are available only at the state level, whereas our main analysis is conducted at the county level; the state-year correlations therefore provide suggestive validation of the mortality signal at a coarser geographic resolution than the identification design requires.

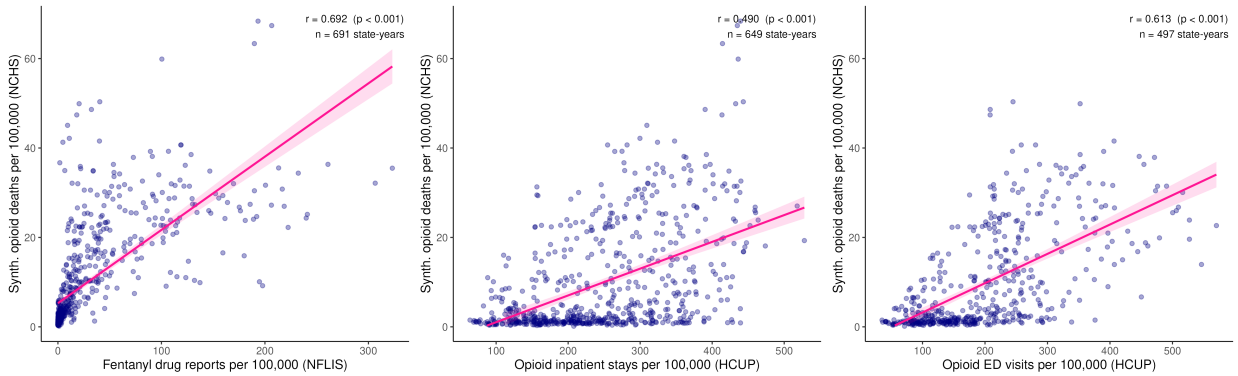


Figure 12: Synthetic Opioid Mortality and Alternative Exposure Measures

Figure 13 provides direct evidence that rising synthetic opioid mortality was accompanied by concurrent growth in public and media salience. The figure plots three measures from 2013 to 2022: Google Trends search interest in the term "fentanyl," the share of online news articles mentioning fentanyl from the Media Cloud news archive, and national synthetic opioid mortality per 100,000 population. Through approximately 2019, all three series co-move closely, indicating that escalating mortality was not occurring in a public information vacuum but was concurrently producing and reflecting growing visibility of the fentanyl crisis. This co-movement is relevant to our identification argument because it indicates that the mortality signals we use to define treatment exposure were salient events in the broader information environment to which providers were exposed. We note that these series are national, while our treatment varies at the county level, so this evidence speaks to the general visibility of the fentanyl crisis and not to variation in local salience across counties. After 2019, the two salience indices diverge from mortality, with deaths accelerating sharply as fentanyl contaminated the stimulant supply. At the same time, search and media attention plateaued or were crowded out by COVID-19 coverage beginning in 2020. This post-2020 divergence does not undermine the salience argument, as the bulk of our treatment cohort crosses its shock threshold before 2020, during the period of tight co-movement.

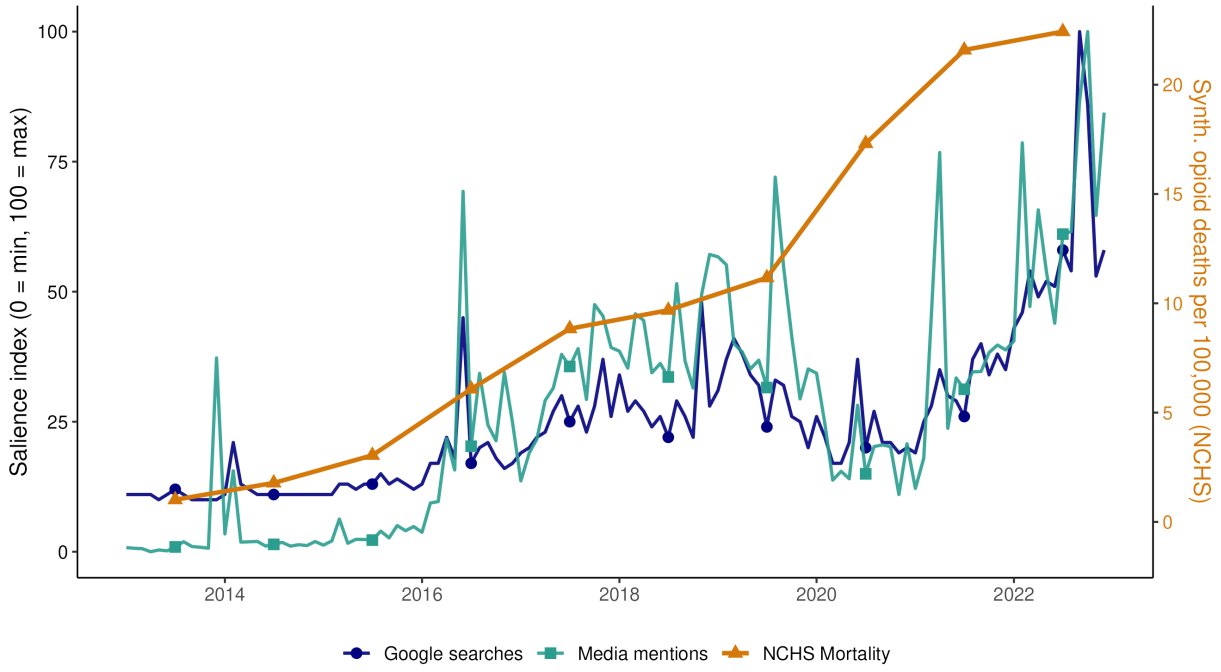


Figure 13: Fentanyl-Related Search Interest, News Coverage, and Synthetic Opioid Mortality, 2013–2022

7 Discussion

7.1 Interpretation

The consistent increase in buprenorphine prescribing following local synthetic opioid crisis onset, robust across three exposure measures and with no evidence of differential pre-trends, supports a causal interpretation of the effect of local crisis onset on the volume of buprenorphine treatment delivered. The response is not attributable to secular trends in drug use or availability, though as Section 7.3 discusses, the county-level outcome reflects both provider and patient decisions. The three measures identify substantially overlapping sets of treated counties (71 percent appear under all three definitions; see Table 1) and should be interpreted as capturing the same underlying phenomenon from different angles rather than as independent replications.

Prior literature found that Medicaid expansion under the ACA, a deliberate and well-

funded policy intervention involving eligibility changes, provider reimbursement, and removal of cost barriers, increased opioid use disorder treatment admissions from Medicaid beneficiaries by 113 percent in early expansion states [Meinhofer and Witman, 2018], with more recent expansions associated with a 21 percent all-payer increase in buprenorphine dispensing [Siegal et al., 2026]. Our estimated effects of 5 to 17 percent are smaller in percentage terms but arise from an organic behavioral shift, without requiring a formal policy change. Moreover, Medicaid expansion occurred in approximately 40 states, whereas synthetic opioids' geographic diffusion eventually reached the vast majority of US counties (Figure 1). An organic response of 5 to 17 percent occurring across nearly all counties may generate a larger aggregate increase in national buprenorphine prescribing than a larger percentage effect confined to expansion states.

An important caveat is that our primary outcome may reflect compositional shifts rather than, or in addition to, provider behavioral change. The outcome decomposition in Section 6.1 addresses this directly. Under first occurrence, both the extensive margin (new prescribers) and the intensive margin (patients per prescriber) contribute to the effect, while the pattern differs across shock definitions, suggesting that different dimensions of crisis exposure activate different margins of provider response.

The heterogeneity results reveal that the prescribing response is concentrated among advanced practice providers, Medicaid-enrolled patients, counties with above-median baseline buprenorphine prescribing, and counties east of the Mississippi River, where synthetic opioids penetrated drug markets earliest. Notably, the mortality data do not allow us to characterize the socioeconomic profile or insurance status of decedents, so we cannot directly link whose deaths triggered the response to who subsequently received treatment. The concentration of the prescribing response in Medicaid is consistent with that being where unmet treatment need was already concentrated, regardless of the demographics of overdose decedents.

Synthetic opioid deaths involving unexpected victims may have served as a community-level signal that heightened provider awareness of the crisis, but the patients who then

presented for or were offered buprenorphine treatment were disproportionately Medicaid-enrolled, because that is where the unmet treatment need was already concentrated. The concentration among APPs and Medicaid patients likely reflects a single underlying channel rather than two independent findings. NPs and PAs disproportionately serve Medicaid-enrolled populations, and Medicaid covers a disproportionate share of individuals with opioid use disorder. The prescribing response therefore flows through the provider-patient dyad most directly exposed to the treatment gap.

The small or null results for commercial insurance and Medicare suggests either that providers serving those populations were already closer to prescribing capacity, that those patients had more alternative treatment pathways (private addiction specialists, cash-pay options), or that the provider types predominantly serving privately insured patients were less responsive to community-level mortality signals. The null result in counties with below-median baseline buprenorphine prescribing is perhaps the most consequential finding, highlighting that the organic provider response builds on existing treatment infrastructure rather than creating it where it did not previously exist.

7.2 Mechanisms

Several mechanisms could drive the provider response. First, providers may directly observe the consequences of untreated OUD among their own patient panels or in emergency department encounters. Second, institutional responses to rising overdose mortality, including public health alerts, hospital protocol changes, and local government initiatives, may create enabling conditions for expanded prescribing. Third, social and professional norms around OUD treatment may shift as the crisis becomes more visible. These provider-side channels do not exhaust the plausible mechanisms as the organic response we document more broadly reflects the joint behavior of multiple actors who together shape local treatment supply. Payer decisions and health-system efforts to improve overdose screening and referral, such as network-adequacy requirements, payment policy for buprenorphine, and proactive engage-

ment of overdose survivors, plausibly operate alongside provider decision-making. Patient treatment-seeking behavior is itself a further channel that local mortality may affect directly. Our analysis cannot isolate any of these specific channels. We note in particular that the two cognitive mechanisms most natural to this setting, salience and rational updating of beliefs about local fentanyl prevalence, are observationally equivalent in our design to a first approximation. Both predict that locally manifest mortality expands prescribing, and both suggest the constraint is in the provider's information environment rather than in regulation or reimbursement. The two diverge only where a signal's vividness and its informational content separate, and the decedent-age results in Section 6.6 speak to that divergence: deaths most likely to generate community alarm, those of young decedents without prior treatment contact, produce no detectable response, while the effects are driven by deaths indicative of a treatable local population. The response therefore is more consistent with the informational value of local mortality than with its capacity to alarm, although as noted in Section 6.1, deaths indicative of a treatable local population also predict greater patient presentation, so this pattern does not by itself separate provider updating from patient demand. What our design cannot establish is whether pre-shock prescribing was low because information about local conditions was genuinely unavailable or because available information was not effective at changing behavior, a distinction on which none of our conclusions can address.

As discussed in Section 2.3, synthetic opioid deaths are qualitatively distinctive in ways that likely amplify their salience relative to earlier crisis waves. They disproportionately involve individuals without prior opioid use history, exposed through contaminated stimulant or counterfeit pill supplies, which may broaden providers' perceptions of who is at risk and reduce stigma around treating opioid use disorder [Tanz et al., 2022, Friedman and Shover, 2023, Perdue et al., 2024]. The heterogeneity results are consistent with a salience mechanism operating through pre-existing treatment capacity rather than through provider type. Advanced practice providers and Medicaid-enrolled patients are where unmet OUD treatment need was already concentrated, so a community-wide mortality signal is more likely

to translate into a prescribing response where providers already have the infrastructure and patient base to act on it. The null result in counties with below-median baseline prescribing suggests that salience alone is insufficient, and provider response requires pre-existing treatment infrastructure to translate awareness into action.

We also note that synthetic opioids increasingly appear in stimulant supplies, and some synthetic opioid-involved deaths may involve individuals whose primary substance use disorder is not opioid-related. The placebo test using non-opioid shocks (Section 6.8) provides indirect evidence on the specificity of the synthetic opioid signal.

7.3 A Secondary Outcome Relevant to the Provider Channel

Our primary outcome measures the quantity of buprenorphine treatment delivered in a county. An increase is consistent with providers becoming more willing to prescribe, with more patients presenting for care, or with both. Because local synthetic opioid mortality plausibly moves patient presentation as well as provider behavior, the buprenorphine result by itself does not isolate the provider margin. This is the central interpretive limitation of our design, and we address it here because one additional outcome is relevant to understanding this further.

If local mortality shocks change how providers think about opioid risk, that reorientation should be visible in a decision that patient presentation does not affect: opioid analgesic prescribing. An inflow of patients seeking treatment for opioid use disorder gives a clinician no reason to write fewer prescriptions for pain, but if the clinician's assessment of local opioid risk changes, then they might prescribe opioids less intensely. This is the county-level analogue of the mechanism documented by Doctor et al. [2018], who find in a randomized setting that prescribers notified of a patient's fatal overdose subsequently reduced their opioid prescribing. We therefore re-estimate our main specifications with county-year opioid analgesic dispensing per 100 residents as the outcome, using the CDC series described in Section 3.3. Appendix Section H reports the estimates.

Opioid analgesic dispensing declines significantly following synthetic opioid shock onset under two of the three shock definitions: first occurrence (-1.32 prescriptions per 100 residents, SE = 0.49, a 1.7 percent decline relative to the pre-treatment mean) and sustained entry (-1.08, SE = 0.48, 1.3 percent). The acute-escalation estimate is small, positive, and not statistically significant (0.80, SE = 0.42).

We interpret this evidence with several qualifications, and we regard it as suggestive rather than decisive.

The interpretation of the two possible findings is asymmetric. A decline in analgesic prescribing following a mortality shock is difficult to generate from patient presentation alone and would support a broader reorientation of clinical posture toward opioids in shocked counties. A null result is considerably less informative, because the analgesic decision is governed by considerations largely absent from the buprenorphine decision, including pain management guidelines, prescription drug monitoring requirements, and litigation exposure. A provider might also reason that deaths driven by illicit fentanyl carry no implication for their own prescribing to pain patients, in which case beliefs about local opioid risk could shift substantially with no analgesic response at all. We therefore do not treat a null on this outcome as evidence against a provider channel. Under this asymmetric logic, the significant declines under first occurrence and sustained entry are the more informative result, consistent with a reorientation of clinical posture toward opioids in shocked counties; the acute-escalation null, given the considerations above, does not weigh against that interpretation.

Three features of the setting further limit inference. First, opioid analgesic prescribing declined nationally and close to monotonically over most of our study period, so this specification asks whether shocked counties declined faster than matched controls rather than whether they declined at all; the common trend is absorbed by period effects, but differential trajectories by county type would not be. Second, several state responses to rising overdose mortality, including must-access prescription drug monitoring mandates, act directly on

analgesic prescribing, so a decline could reflect a policy response to the same shock rather than individual clinician updating. We control for these policies as described in Section 6.7, but the timing of state responses to local mortality is not fully observable at the county level. Third, the two outcomes are not independent: a contraction in analgesic supply may itself push some patients toward treatment for opioid use disorder, which would generate a negative analgesic estimate and a positive buprenorphine estimate through a channel that involves no change in provider beliefs about buprenorphine.

The county-level prescriber population writing opioid analgesics overlaps only partially with the population prescribing buprenorphine, so this test speaks to clinical posture in the county as a whole rather than to the behavior of the specific providers driving our main result.

7.4 Relation to Existing Literature

These findings complement work on supply-side barriers to buprenorphine prescribing [Stein et al., 2016, Dick et al., 2015, Stein et al., 2015, 2021, Miles et al., 2023, Nguyen et al., 2022] by identifying a demand-side channel through which local crisis severity shapes provider behavior. The geographic mismatch between community need and buprenorphine provider capacity that motivates this channel is well-documented. Haffajee et al. [2019] show that US counties with the highest opioid overdose mortality are systematically among those with the lowest capacity to deliver medication-assisted treatment, and Andrilla et al. [2019] document persistent rural gaps in DEA-waivered provider availability. Our findings offer a partial resolution to this puzzle by noting that where baseline prescribing infrastructure exists, local synthetic opioid mortality is associated with an expansion of treatment volume, consistent with the concentration of effects we observe in above-median baseline counties. In the lowest-capacity counties, no organic response emerges, indicating that the organic channel does not operate where the market has not yet established a treatment foothold. The concentration of effects among Medicaid patients connects to Meinhofer and Witman

[2018] and Siegal et al. [2026] and suggests that synthetic opioid-driven mortality may have catalyzed provider use of existing Medicaid coverage infrastructure, potentially amplifying the reach of expansion itself. Our work also connects to Nguyen et al. [2021], who document COVID-era shifts in buprenorphine dispensing patterns, and to Gupta et al. [2023], who study competitive spillovers from opioid prescribing restrictions. Pacula et al. [2025] provide a broader methodological framework for evaluating opioid crisis interventions within which our channel fits.

Methodologically, our approach adapts the consecutive-period design of Evans et al. [2022], who identifies crack cocaine market penetration using consecutive years with cocaine deaths. We apply this logic to synthetic opioids at a quarterly frequency, which better captures the rapid escalation of fentanyl mortality. The two settings also differ in the direction of the behavioral response. Evans examines criminal market expansion, whereas we examine a treatment supply response. Our finding that the sustained-entry measure requiring three consecutive quarters of deaths produces the largest effect echoes the intuition that consecutive-period thresholds identify entrenched rather than incidental exposure.

7.5 Limitations

Several limitations warrant discussion. We cannot entirely rule out confounders coinciding with treatment onset. The balance analysis in Table 2 reveals that treated counties are more urban and larger than matched controls. While we assess robustness to conditioning on these variables in the doubly robust estimation step, unobservable confounders that coincide with synthetic opioids' arrival remain a concern. Our outcome captures filled prescriptions, which may differ from medication adherence or clinical outcomes. IQVIA data may underrepresent prescribing in rural counties, and 25 to 43 percent of treated counties fail to match within the caliper across shock definitions, with unmatched counties tending to be smaller and more rural. Our estimates therefore generalize primarily to larger counties. County-quarter level analysis may mask within-county heterogeneity in provider response. We do

not observe the specific mechanisms through which providers respond, and the distinction between information salience, institutional channels, and norm shifts remains unresolved. More fundamentally, our primary outcome cannot separate a change in provider behavior from a change in patient presentation, since local synthetic opioid mortality plausibly affects both. Section 7.3 presents a secondary outcome bearing on this question, and the new-prescriber-entry results in Section 6.1 and the null in counties with below-median baseline prescribing are both more readily explained by a provider margin than by patient flow alone, but none of these are decisive and we do not claim to identify the provider channel in isolation. While we interpret the null result in low-baseline counties as evidence that the organic response requires existing infrastructure, an alternative explanation is that our outcome measure lacks power to detect small effects in counties with very low prescribing rates.

7.6 Implications for Understanding Treatment Supply

Our findings carry several implications for understanding how treatment supply adjusts during drug crises. The existence of an organic provider response to local overdose mortality indicates that the visibility of mortality information is itself a determinant of prescribing, and that this response operates with a lag relative to the underlying deaths. The monotonic growth of treatment effects over time indicates that the response deepens with sustained exposure. These parameters are relevant inputs for evaluating information-based approaches such as overdose surveillance dashboards and prescriber notification, whose experimental analogue at the patient level is studied by Doctor et al. [2018].

The concentration of effects among advanced practice providers and Medicaid patients highlights that NPs and PAs are the front-line responders to the crisis in underserved communities. The organic response we document therefore operates through the provider segment whose prescribing authority is most directly governed by scope-of-practice rules. The elimination of the X-waiver requirement in January 2023 removed a key barrier for these providers,

and our findings suggest that crisis exposure may have been an important motivator for APPs to begin using that expanded prescribing authority.

The null result in counties with low baseline buprenorphine prescribing implies that the organic provider response does not operate where prescribing infrastructure is absent. Synthetic opioid deaths alone do not generate a prescribing response where no prescribing capacity previously existed. In these communities, which are disproportionately rural and underserved, the crisis signal goes unanswered. Any information channel therefore has an infrastructure precondition: the counties where the treatment gap is widest are those where the mechanism we document contributes least.

This infrastructure precondition is unlikely to be resolved by the expansion of telemedicine options for buprenorphine that began during the COVID-19 pandemic. Despite the availability of virtual-only prescribing models, most patients initiating or continuing buprenorphine treatment still receive care through traditional, in-person clinician relationships. Among privately insured and Medicare Advantage patients, only 3.2 percent received care under a virtual-only model [Mehrotra et al., 2026]. Areas that are effectively buprenorphine deserts at baseline may therefore remain unable to respond to rising local need even as remote-care options expand, reinforcing the importance of directly identifying and addressing gaps in physical treatment infrastructure.

8 Conclusion

The literature on buprenorphine access has focused primarily on supply-side constraints: regulatory barriers and training requirements [Stein et al., 2016, Dick et al., 2015], stigma [Van Boekel et al., 2013], and reimbursement inadequacy [Meinhofer and Witman, 2018]. This paper identifies a complementary demand-side channel. Exploiting the staggered geographic diffusion of synthetic opioids across US counties from 2013 through 2023, we show that local synthetic opioid mortality causes an expansion in the volume of buprenorphine

treatment delivered, organically and without formal policy intervention. This volume response reflects both provider prescribing decisions and patient presentation for care. The increase in the number of unique prescribers indicates the provider margin contributes, although does not rule out a concurrent increase in patient presentation. The response is consistent across three exposure measures, represents a 5 to 17 percent increase from pre-treatment baselines, and grows monotonically over time, indicating durable behavioral change, not a transient adjustment.

The heterogeneity in our findings carries implications beyond the average effect. The prescribing response is concentrated among advanced practice providers, Medicaid patients, communities that already had some buprenorphine prescribing infrastructure, and counties east of the Mississippi River, where the synthetic opioid supply arrived earliest. Counties with little baseline prescribing capacity showed no significant response. This pattern suggests that synthetic opioid mortality activates existing treatment capacity instead of creating it from scratch, and that the organic response we document is absent where treatment infrastructure does not yet exist.

These findings identify a channel through which local crisis severity expands the volume of OUD treatment delivered. Local mortality information emerges as a determinant of treatment volume, consistent with experimental evidence that directly informing prescribers of patients' fatal overdoses shifts prescribing [Doctor et al., 2018], and the response operates only where prescribing infrastructure already exists. As synthetic opioids reach virtually every US county, the communities where no response has yet emerged are those where the treatment gap is deepest and the organic channel offers the least.

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Appendix

A. Matching Performance Diagnostics

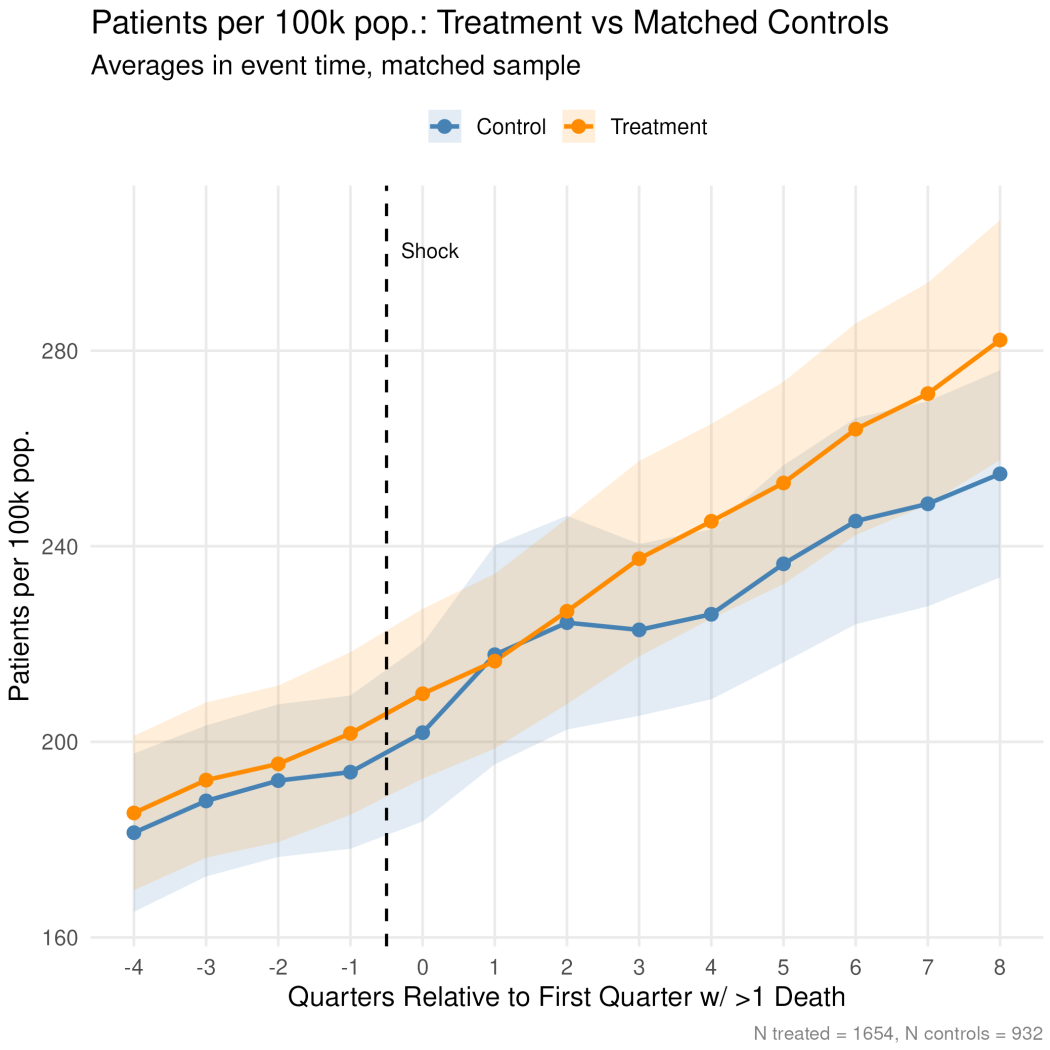

Figure A1: Matching Performance: First Occurrence

Notes: IQVIA LRx data (2013–2023), county-quarter level. Controls matched on pre-period prescribing mean, trend, SD, and log population. Treatment: first quarter with >1 synthetic opioid death. Ribbons = 95% CIs.

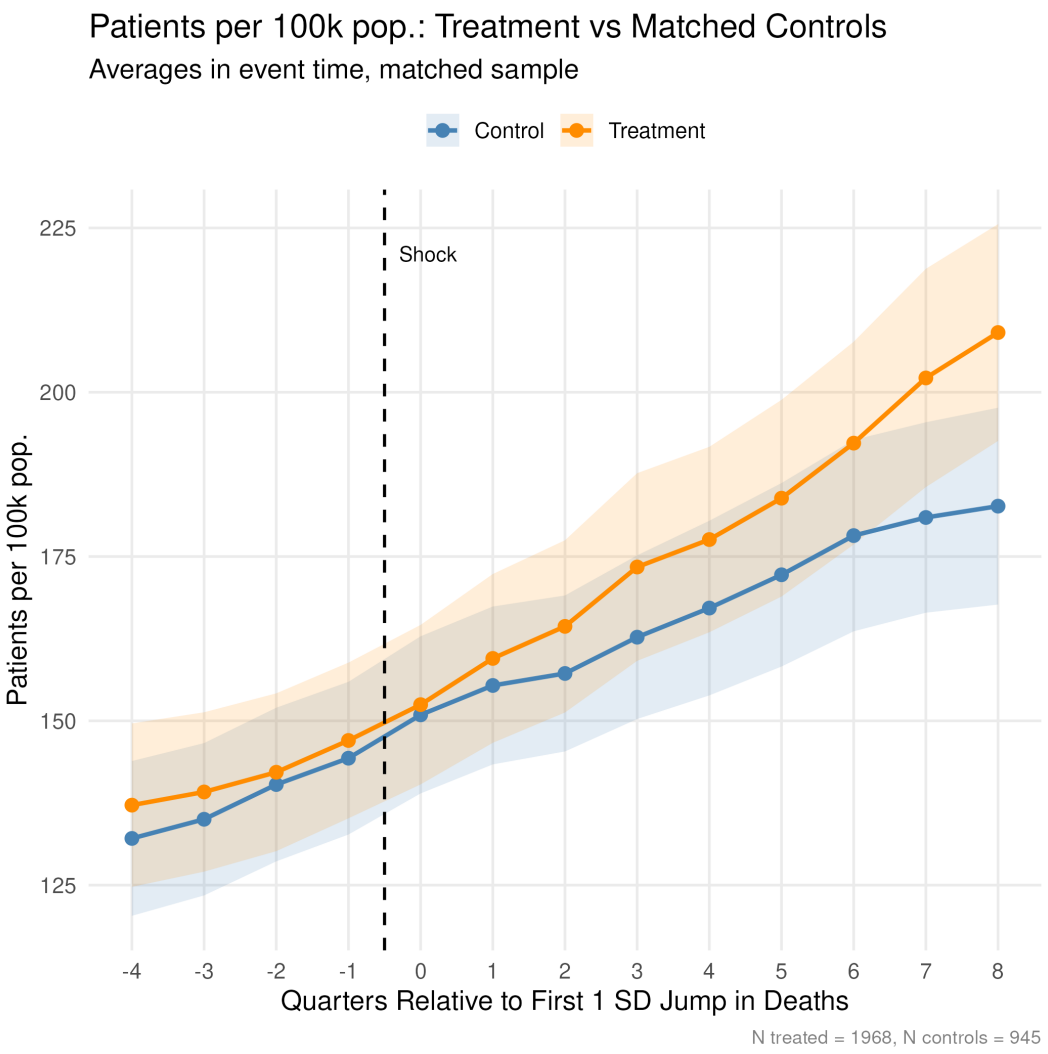

Figure A2: Matching Performance: Acute Escalation

Notes: IQVIA LRx data (2013–2023), county-quarter level. Controls matched on pre-period prescribing mean, trend, SD, and log population. Treatment: first quarter exceeding county 4-quarter rolling mean by 1 SD.

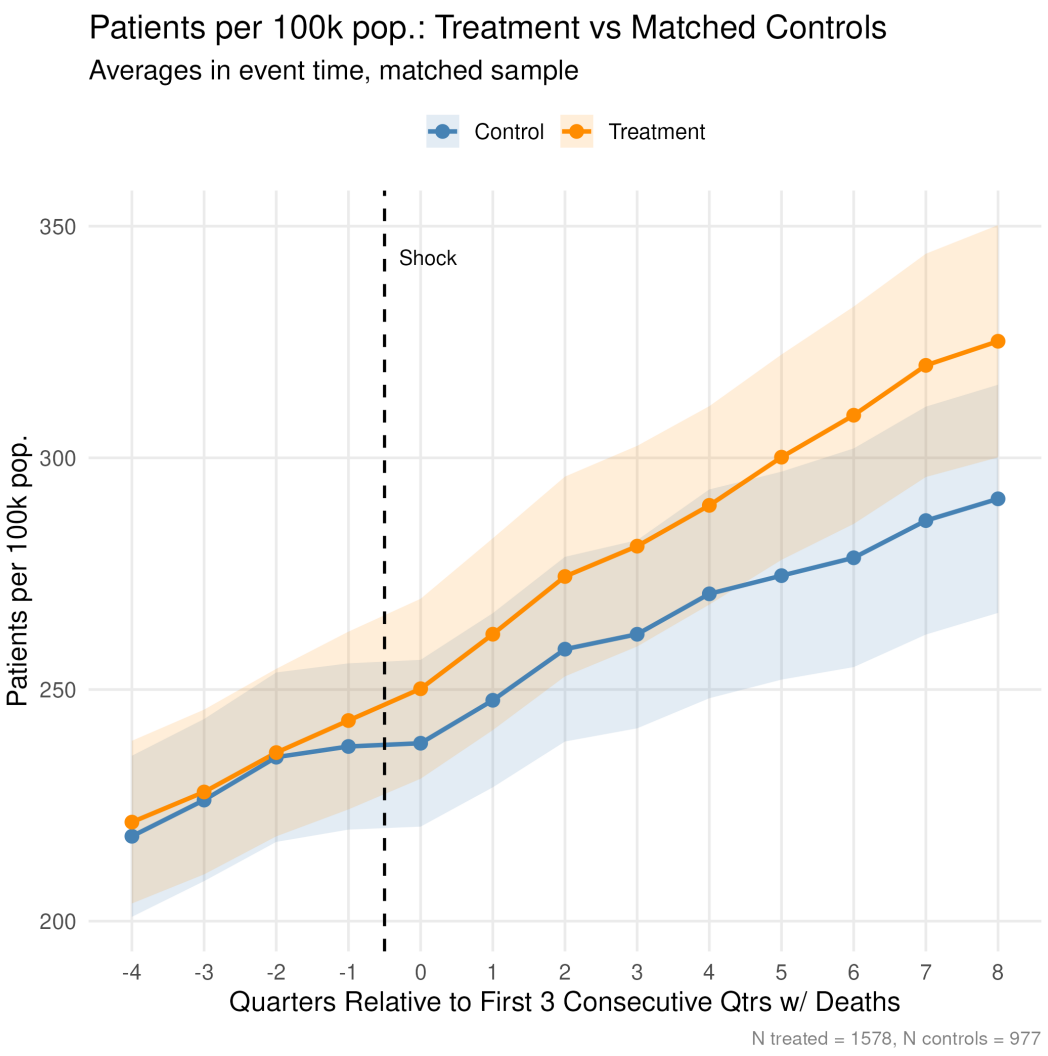

Figure A3: Matching Performance: Sustained Entry

Notes: IQVIA LRx data (2013–2023), county-quarter level. Controls matched on pre-period prescribing mean, trend, SD, and log population. Treatment: first 3 consecutive quarters with $\geq$1 death.

B. Balance Results for Alternative Shock Definitions

First Occurrence

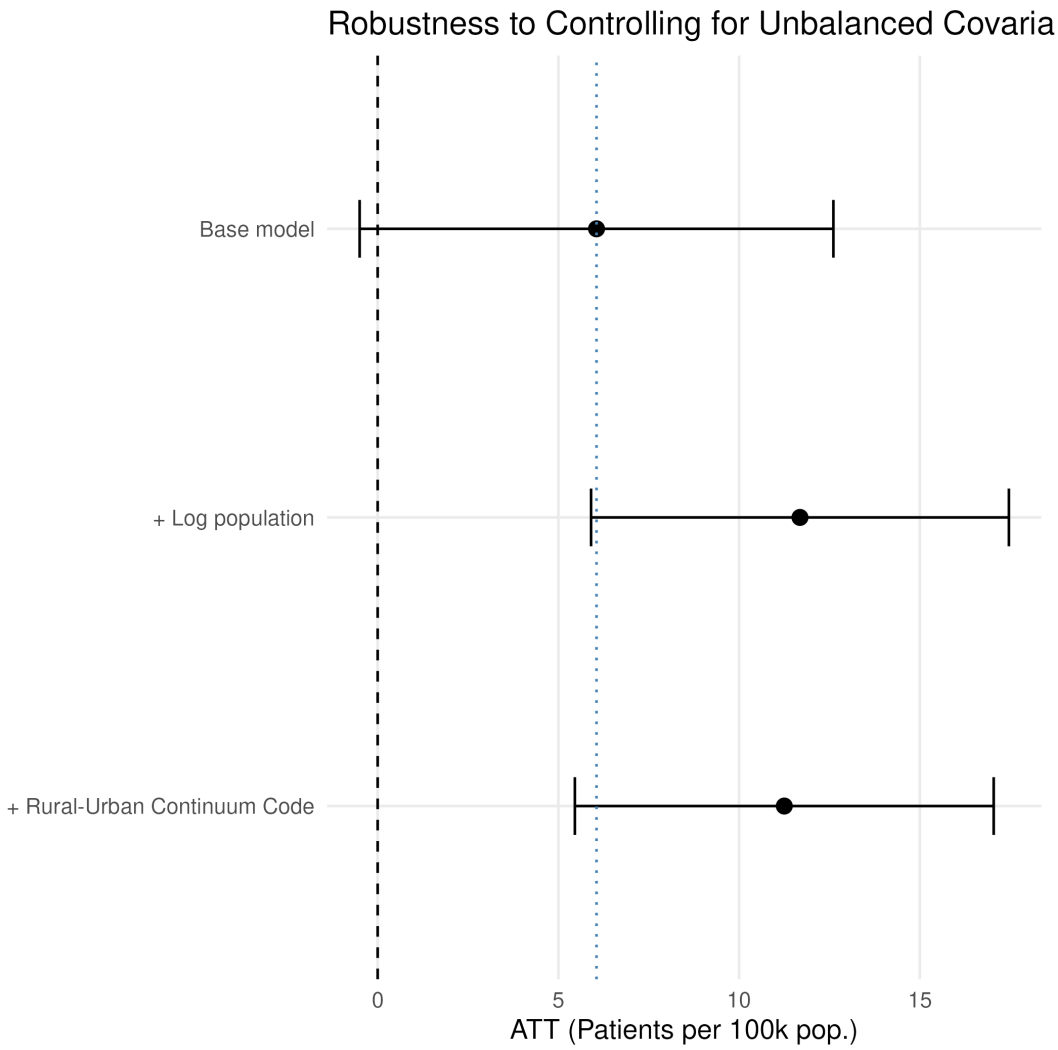

Figure A4: Controlling for Unbalanced Variables: First Occurrence

Notes: IQVIA LRx data, matched county-quarter panel, first-occurrence shock definition. Each row adds one variable failing the balance check in Table 2 (normalized difference $\geq$0.25) to the doubly robust estimation step, on top of the base specification (no controls) and the main specification (log population only). Points are the overall ATT under each specification; horizontal bars are 95% bootstrap confidence intervals (county-clustered, 5,000 replications). The dashed black line marks zero; the dotted steelblue line marks the base-model (no-controls) ATT, for reference. Estimates are stable across specifications, indicating the main result is not driven by the covariates on which treated and matched control counties remain imbalanced.

Acute Escalation

Table A1: Balance on County Characteristics: Treated vs. Matched Control Counties

	Treated		Control		Norm.
	Mean	SD	Mean	SD	Diff.
Matching variables					
Pre-period mean Bup. patients/100K	140.95	252.32	137.71	243.91	0.009
Pre-period Bup. prescribing trend	3.45	44.24	4.24	41.60	-0.013
Pre-period Bup. prescribing SD	22.88	61.29	22.39	57.81	0.006
Healthcare market characteristics					
Total physicians per 100,000	152.44	157.66	129.52	237.90	0.080
Primary care physicians per 100,000	73.28	59.97	69.67	95.63	0.032
Opioid Rx rate per 100	72.15	46.86	66.67	50.37	0.080
Hospital beds per 1,000 population	5.28	5.66	7.32	9.98	-0.177
Socioeconomic characteristics					
Log population	10.52	1.15	9.68	1.03	0.549
Percent non-Hispanic Black	10.62	15.17	9.34	16.00	0.058
Percent Hispanic	8.68	12.58	9.75	14.79	-0.055
Percent age 18–44	30.16	4.28	28.94	4.04	0.206
Poverty rate (%)	16.01	5.93	16.29	6.88	-0.030
Uninsured rate (%)	12.80	5.01	14.24	5.40	-0.195
Median household income ($)	51,252.17	13,080.63	49,548.28	12,359.33	0.095
Pre-existing drug market indicators					
Rural-Urban Continuum Code	4.83	2.75	6.35	2.60	-0.402
Heroin death rate per 100,000	0.18	0.48	0.08	0.39	0.169
Non-synthetic drug OD rate per 100,000	2.40	2.48	2.03	2.52	0.106
Interstate highway within county (0/1)	0.48	0.50	0.35	0.48	0.191

Notes: Balance presented for the acute escalation shock definition. Normalized differences calculated as the difference in means divided by the square root of the sum of variances. Values below 0.25 in absolute value are generally considered adequate balance [Imbens and Rubin, 2016]. Healthcare market characteristics are from NPPES (physician counts), the CDC Opioid Dispensing Rate Maps (opioid dispensing rate), and the CMS Provider of Services file (hospital beds per 1,000 population). Socioeconomic characteristics are from SEER (population, race/ethnicity and age shares), Census SAIPE (poverty rate and median household income), and Census SAHIE (uninsured rate). The Rural-Urban Continuum Code is from the USDA Economic Research Service. Pre-existing drug mortality rates are from NCHS mortality microdata. The interstate highway indicator is constructed from U.S. Census Bureau TIGER/Line Shapefiles.

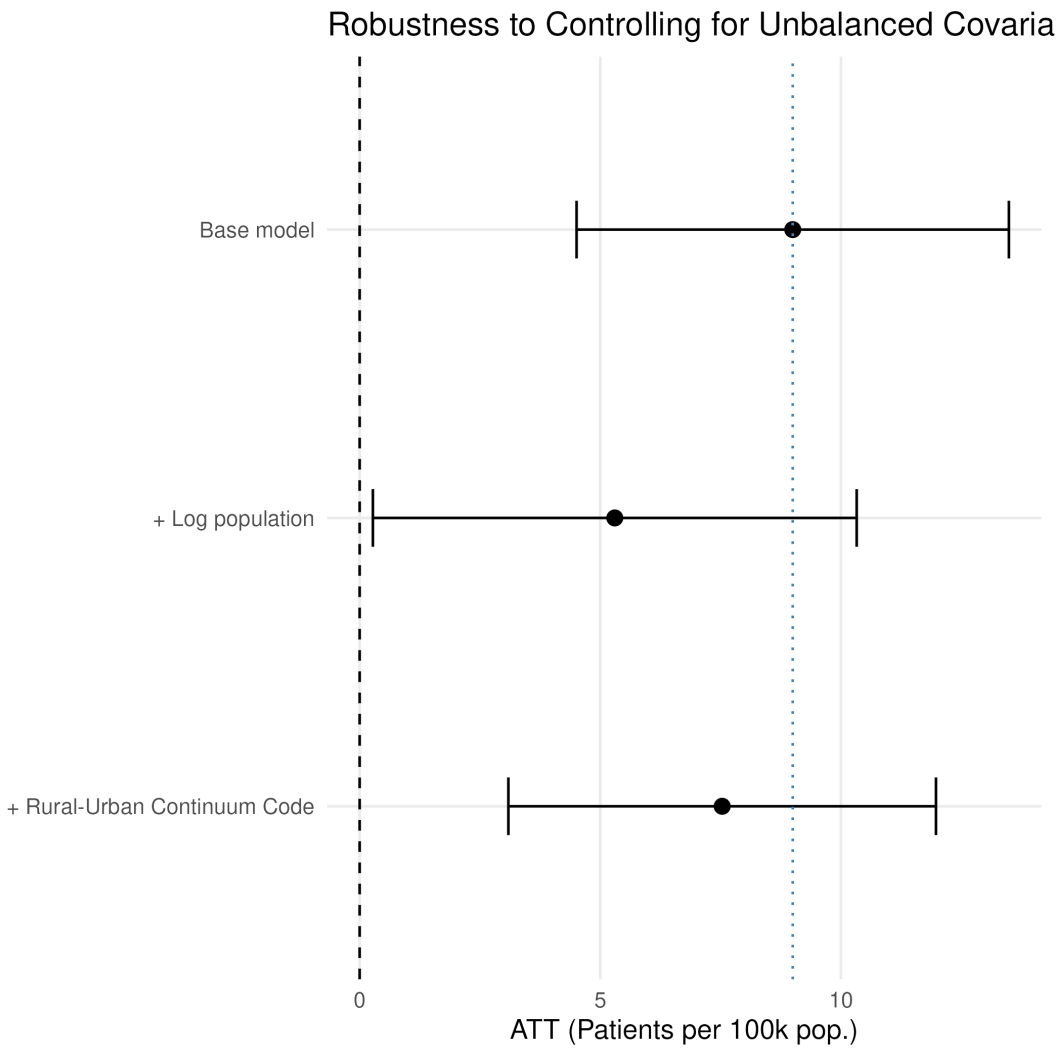

Figure A5: Controlling for Unbalanced Variables: Acute Escalation

Notes: IQVIA LRx data, matched county-quarter panel, acute-escalation shock definition. Each row adds one variable failing the balance check in Table A1 (normalized difference $\geq$0.25) to the doubly robust estimation step, on top of the base specification (no controls) and the main specification (log population only). Points are the overall ATT under each specification; horizontal bars are 95% bootstrap confidence intervals (county-clustered, 5,000 replications). The dashed black line marks zero; the dotted steelblue line marks the base-model (no-controls) ATT, for reference.

Sustained Entry

Table A2: Balance on County Characteristics: Treated vs. Matched Control Counties

	Treated		Control		Norm.
	Mean	SD	Mean	SD	Diff.
Matching variables					
Pre-period mean Bup. patients/100K	231.28	356.52	228.47	348.77	0.006
Pre-period Bup. prescribing trend	8.12	49.87	7.39	48.68	0.010
Pre-period Bup. prescribing SD	35.10	69.13	35.57	67.94	-0.005
Healthcare market characteristics					
Total physicians per 100,000	178.15	159.41	159.37	425.61	0.041
Primary care physicians per 100,000	82.17	60.66	78.99	152.87	0.019
Opioid Rx rate per 100	66.10	41.40	65.11	51.38	0.015
Hospital beds per 1,000 population	4.81	4.64	6.67	7.37	-0.214
Socioeconomic characteristics					
Log population	10.89	1.00	9.94	1.00	0.667
Percent non-Hispanic Black	10.61	14.37	9.76	15.58	0.040
Percent Hispanic	8.30	11.29	8.91	12.43	-0.036
Percent age 18–44	30.52	4.02	29.74	4.50	0.130
Poverty rate (%)	14.99	5.33	16.25	6.31	-0.153
Uninsured rate (%)	11.24	4.50	12.95	4.84	-0.259
Median household income ($)	54,852.36	13,880.01	50,967.44	12,756.46	0.206
Pre-existing drug market indicators					
Rural-Urban Continuum Code	4.15	2.55	6.06	2.56	-0.529
Heroin death rate per 100,000	0.20	0.45	0.09	0.38	0.196
Non-synthetic drug OD rate per 100,000	2.71	2.39	2.13	2.41	0.169
Interstate highway within county (0/1)	0.56	0.50	0.37	0.48	0.276

Notes: Balance presented for the sustained entry shock definition. Normalized differences calculated as the difference in means divided by the square root of the sum of variances. Values below 0.25 in absolute value are generally considered adequate balance [Imbens and Rubin, 2016]. Healthcare market characteristics are from NPPES (physician counts), the CDC Opioid Dispensing Rate Maps (opioid dispensing rate), and the CMS Provider of Services file (hospital beds per 1,000 population). Socioeconomic characteristics are from SEER (population, race/ethnicity and age shares), Census SAIPE (poverty rate and median household income), and Census SAHIE (uninsured rate). The Rural-Urban Continuum Code is from the USDA Economic Research Service. Pre-existing drug mortality rates are from NCHS mortality microdata. The interstate highway indicator is constructed from U.S. Census Bureau TIGER/Line Shapefiles.

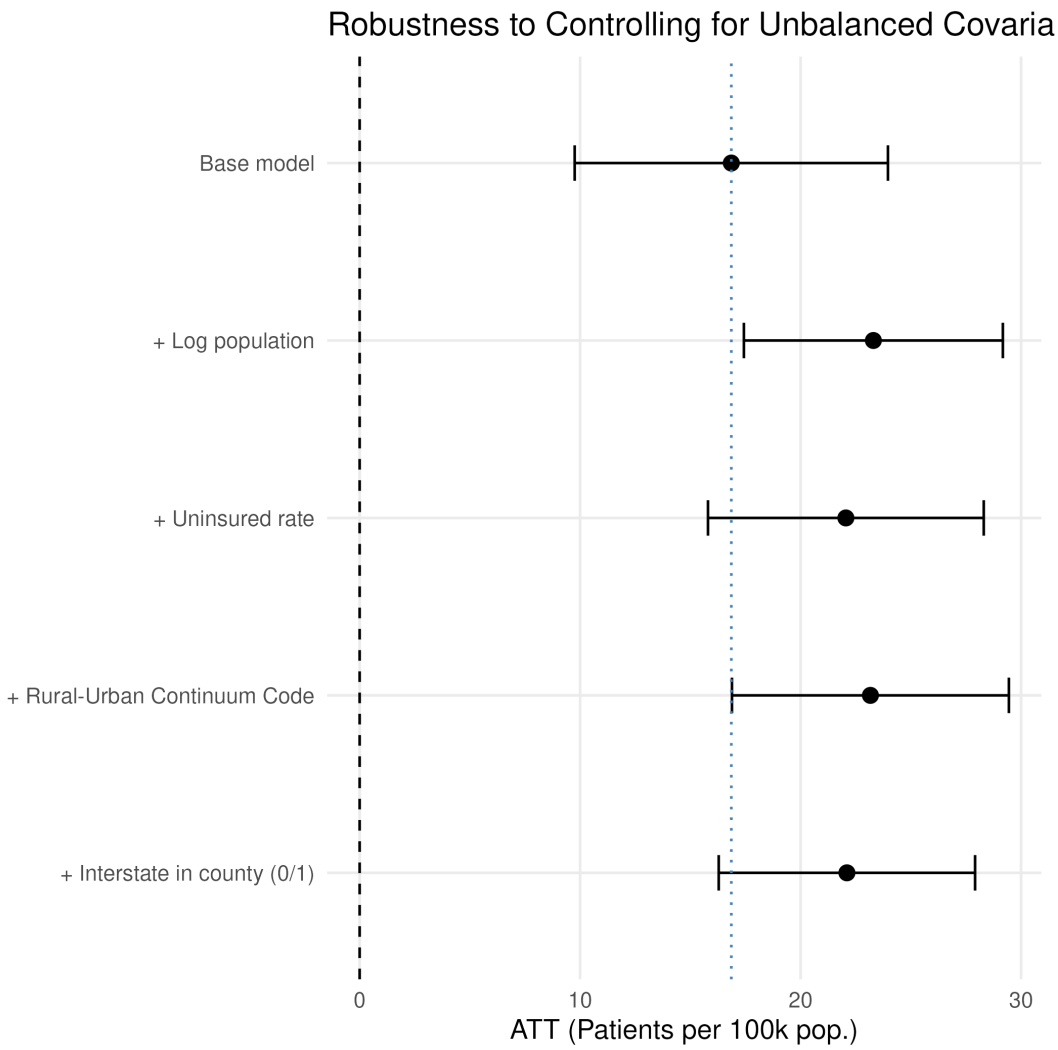

Figure A6: Controlling for Unbalanced Variables: Sustained Entry

Notes: IQVIA LRx data, matched county-quarter panel, sustained-entry shock definition. Each row adds one variable failing the balance check in Table A2 (normalized difference $\geq$0.25) to the doubly robust estimation step, on top of the base specification (no controls) and the main specification (log population only). Points are the overall ATT under each specification; horizontal bars are 95% bootstrap confidence intervals (county-clustered, 5,000 replications). The dashed black line marks zero; the dotted steelblue line marks the base-model (no-controls) ATT, for reference.

C. Comparison Group by Shock Definition

Table A3: Comparison Group Size by Treatment Cohort - Acute Escalation

Cohort Year	Treated Counties	Available Comparisons	Matched Controls
2013	242	2011	214
2014	270	1830	227
2015	232	1622	205
2016	202	1407	170
2017	207	1247	176
2018	151	1139	123
2019	102	1002	88
2020	147	836	121
2021+	415	2324	324

Notes: Reported for the acute-escalation shock definition.

Table A4: Comparison Group Size by Treatment Cohort - Sustained Entry

Cohort Year	Treated Counties	Available Comparisons	Matched Controls
2013	55	2578	54
2014	113	2478	110
2015	131	2320	125
2016	181	2124	165
2017	185	1988	175
2018	126	1870	116
2019	103	1732	100
2020	169	1516	151
2021+	515	4827	463

Notes: Reported for the sustained entry shock definition.

D. Bootstrap Inference Diagnostics

The main specifications are estimated with bootstrap standard errors clustered by county using 5,000 replications. The number of unique county clusters is 2,586 (first occurrence), 2,913 (acute escalation), and 2,555 (sustained entry). To assess sensitivity to the number of bootstrap draws, we re-estimated each specification with 1,000 replications. Table A5 reports the comparison. The 95% confidence intervals under 1,000 replications are [5.96, 17.41], [0.20, 10.40], and [17.44, 29.16] for the first occurrence, acute escalation, and sustained entry definitions, respectively, compared to [5.90, 17.46], [0.28, 10.32], and [17.42, 29.18] under 5,000 replications. The maximum difference in CI width across all three specifications is 0.163 buprenorphine patients per 100,000 population; the choice between 1,000 and 5,000 replications has no meaningful effect on inference.

Table A5: Bootstrap Stability: 1,000 vs. 5,000 Replications

				95% CI		
Specification	Clusters	Treated	ATT	1,000 reps	5,000 reps	Δ Width
First occurrence (>1 death)	2,586	1,654	11.68***	[5.96, 17.41]	[5.90, 17.46]	-0.115
Acute escalation (z-score)	2,913	1,968	5.30*	[0.20, 10.40]	[0.28, 10.32]	+0.163
Sustained entry (3 consec.)	2,555	1,578	23.30***	[17.44, 29.16]	[17.42, 29.18]	-0.038

Notes: ATT point estimates from the 5,000-replication bootstrap used in main results. Confidence intervals equal 1.96 times the bootstrap standard error, clustered by county. Δ Width is the CI width under 1,000 replications minus the CI width under 5,000 replications. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

We also check sensitivity to two features of the estimation procedure held fixed in the main specifications. First, the matched samples use a caliper of 1 standard deviation in propensity-score space (Section 4.3). Table A6 re-estimates each shock definition across calipers ranging from 0.5 to 2 standard deviations in increments of 0.25. Point estimates are stable across this range for all three shock definitions, with overlapping confidence intervals

throughout and no evidence that the main caliper choice is an outlier within the range considered.

Table A6: Robustness to Matching Caliper

Shock / Caliper	N Treated	N Controls	ATT	95% CI
Panel A: First occurrence				
Caliper = 0.5	1,648	926	11.95***	[6.19, 17.72]
Caliper = 0.75	1,652	927	10.87***	[5.06, 16.67]
Caliper = 1 (main)	1,654	932	11.68***	[5.90, 17.47]
Caliper = 1.25	1,654	933	12.66***	[6.89, 18.44]
Caliper = 1.5	1,655	933	13.08***	[7.29, 18.87]
Caliper = 1.75	1,656	936	12.49***	[6.68, 18.30]
Caliper = 2	1,656	935	12.55***	[6.75, 18.35]
Panel B: Acute escalation				
Caliper = 0.5	1,964	936	5.13*	[0.39, 9.87]
Caliper = 0.75	1,966	943	4.29	[-0.58, 9.16]
Caliper = 1 (main)	1,968	945	5.30*	[0.24, 10.36]
Caliper = 1.25	1,970	946	5.12*	[0.11, 10.14]
Caliper = 1.5	1,970	944	5.56*	[0.54, 10.57]
Caliper = 1.75	1,972	948	4.51	[-0.81, 9.84]
Caliper = 2	1,972	947	4.12	[-1.25, 9.50]
Panel C: Sustained entry				
Caliper = 0.5	1,576	961	23.81***	[17.72, 29.90]
Caliper = 0.75	1,578	971	22.25***	[16.34, 28.17]
Caliper = 1 (main)	1,578	977	23.30***	[17.41, 29.19]

Continued on next page

Table A6 – *continued*

Shock / Caliper	N Treated	N Controls	ATT	95% CI
Caliper = 1.25	1,579	977	23.01***	[17.14, 28.89]
Caliper = 1.5	1,580	975	21.78***	[15.88, 27.68]
Caliper = 1.75	1,581	976	21.16***	[15.24, 27.07]
Caliper = 2	1,582	976	21.59***	[15.68, 27.50]

Second, our main specifications cluster standard errors at the county level, consistent with the level at which treatment timing is assigned. Given the well-documented geographic clustering of synthetic opioid diffusion along trafficking corridors, correlated shocks across counties within a state could understate the appropriate standard errors. Table A7 re-estimates the caliper-1 specification with standard errors clustered at the state level instead. Point estimates are unchanged, as expected since clustering only affects inference. Confidence intervals widen under state clustering, reflecting the much smaller number of state relative to county clusters; the first-occurrence and sustained-entry estimates remain significant, while the acute-escalation estimate, already only marginally significant under county clustering, loses significance under the coarser state-level clustering.

Table A7: Robustness to State-Level Clustering

		95% CI		
Shock	ATT	County-clustered	State-clustered	N Treated
First occurrence	11.68***	[5.89, 17.47]	[2.62, 20.75]	1,654
Acute escalation	5.30*	[0.27, 10.33]	[-0.42, 11.02]	1,968
Sustained entry	23.30***	[17.41, 29.19]	[15.97, 30.63]	1,578

Notes: Estimator: Callaway–Sant'Anna (2021), doubly robust, matched county-quarter panel, caliper=1, 5,000 bootstrap iterations. County-clustered is the specification used throughout the paper; state-clustered collapses SEs to the (much smaller) number of state clusters. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

E. Heterogeneity Results

Table A8: Heterogeneity in Treatment Effects Across Shock Measures

	First Occurence	Acute Escalation	Sustained Entry
Subgroup	ATT	ATT	ATT
By urbanicity			
Metropolitan counties (RUCC 1–3)	2.84	0.22	22.81***
	(3.81)	(2.29)	(3.58)
Non-metropolitan counties (RUCC 4–9)	21.11***	9.97**	22.51***
	(3.44)	(3.58)	(3.99)
By payer			
Cash pay	-1.08	-0.88	3.89***
	(0.71)	(0.47)	(0.62)

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Table A8 – *continued*

Subgroup	First Occurence ATT	Acute Escalation ATT	Sustained Entry ATT
Commercial	2.37	0.94	6.34***
	(1.22)	(1.41)	(1.19)
Medicare	-0.21	0.94**	0.88*
	(0.34)	(0.32)	(0.38)
Medicaid	9.36***	3.64**	14.48***
	(2.04)	(1.30)	(2.17)
By provider specialty			
Primary care	3.08	-1.51	8.01***
	(1.60)	(2.20)	(1.65)
Psychiatry	2.28***	1.28*	1.65*
	(0.65)	(0.52)	(0.65)
Emergency	-0.89	-0.52	-0.20
	(0.56)	(0.40)	(0.68)
APP	9.15***	6.12***	16.08***
	(1.78)	(1.58)	(2.37)
Other	-1.28	-0.11	-1.67
	(1.72)	(0.61)	(0.89)
By baseline overdose burden			
Above-median accidental drug OD rate	19.49***	9.89**	29.90***
	(4.21)	(3.65)	(4.98)

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Table A8 – *continued*

Subgroup	First Occurence ATT	Acute Escalation ATT	Sustained Entry ATT
Below-median accidental drug OD rate	7.15*	1.16	19.34***
	(2.91)	(2.63)	(2.34)
By baseline buprenorphine prescribing			
Above-median Bup. rate	22.35***	18.18***	34.07***
	(3.97)	(3.81)	(4.07)
Below-median Bup. rate	1.92	-6.27**	14.07***
	(3.18)	(2.21)	(3.56)

Notes: Standard errors in parentheses. Columns compare three shock definitions: first quarter with >1 synthetic opioid death, first quarter exceeding 1 SD above baseline, and first quarter of three consecutive quarters with synthetic opioid deaths. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

F. Unmatched CS-DiD

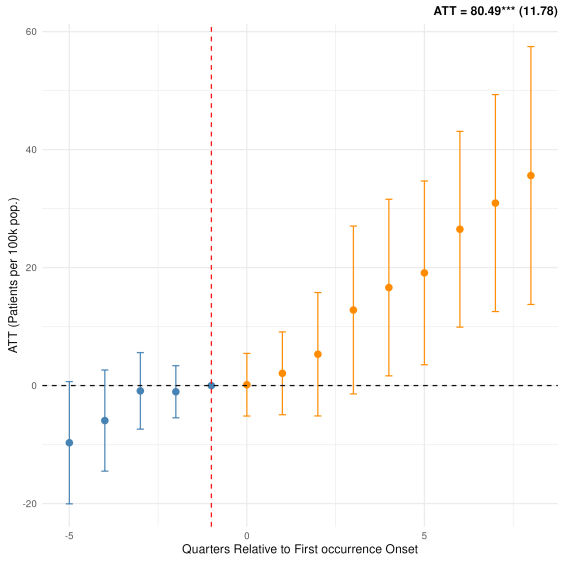
Table A9 reports the overall ATT under each shock definition re-estimated on the full, unmatched panel (Callaway–Sant'Anna, doubly robust, using log population covariate, not-yet-treated controls, universal base period, 5,000 bootstrap iterations), addressing the regression-to-the-mean concern raised in Section 4.3 [Daw and Hatfield, 2018]. Compare to Table 4 (matched sample). The unmatched estimates are substantially larger and less precise than the matched estimates: 80.49 (SE = 11.78) vs. 11.68 (SE = 2.95) under first occurrence, 48.10 (SE = 32.72, not significant) vs. 5.30 (SE = 2.56) under acute escalation, and 111.17 (SE = 14.63) vs. 23.30 (SE = 3.00) under sustained entry. Figure A7 additionally shows a downward pre-period drift under first occurrence and sustained entry, though no individual pre-period coefficient is statistically significant; the pattern is flat under acute escalation.

Table A9: Average Treatment Effect on the Treated: Unmatched Sample

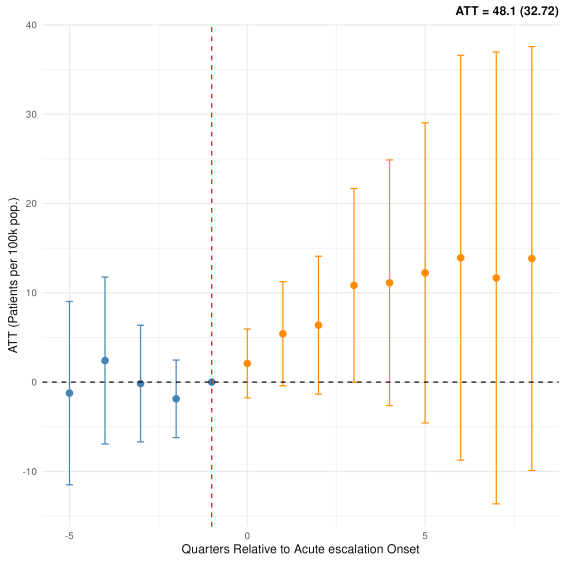
	(1) First occurrence	(2) Acute escalation	(3) Sustained entry
ATT	80.49***	48.10	111.17***
	(11.78)	(32.72)	(14.63)
Pre-treatment mean	149	120	185
Percent effect	54.17%	40.17%	59.94%
Treated counties	1694	2083	1625
Never-treated counties	869	541	1154
County-quarter obs.	123,004	125,932	133,372
Estimator	Callaway–Sant'Anna (2021), doubly robust		
Control group	Not-yet-treated		
SE clustering	County, 5,000 bootstrap iterations		

Notes: No propensity-score/Mahalanobis matching step; full panel, not-yet-treated controls. Compare to Table 4 (matched sample). $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

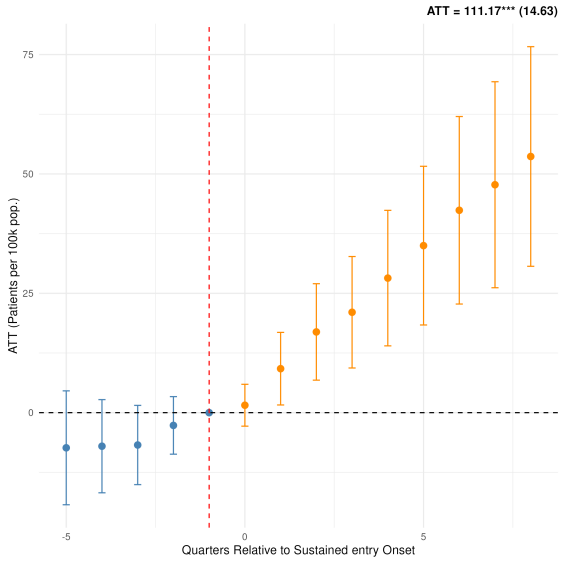
The matched control counties and the permanently never-treated subset of the not-yet-treated pool used in Table A9 differ most on log population and the Rural-Urban Continuum Code, in the same direction as, and more severely than, the treated-versus-matched-controls imbalance already documented in Table 2, and on baseline prescribing levels, which are



(a) First Occurrence



(b) Acute Escalation



(c) Sustained Entry

Figure A7: Event-Study Estimates, Unmatched Sample

Notes: Same specification as Figure 2, estimated on the full unmatched panel with not-yet-treated controls. Blue = pre-treatment; orange = post-treatment. Bars = 95% CIs. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

roughly twice as high among matched controls. The never-treated pool is therefore not simply a noisier version of the matched control set: it is systematically smaller, more rural, and less prescribing-intensive at baseline, consistent with the magnitude gap between the matched and unmatched ATT estimates in Table A9. Table A10 reports the full covariate comparison underlying this claim.

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Table A10: County Characteristics: Matched Controls vs. Never-Treated Pool

	Matched controls	Never-treated pool	Norm. diff.
First occurrence (N matched = 932, N never-treated = 869)			
Patients per 100,000 (time-avg.)	214.71	88.81	0.323
Log population	9.86	9.06	0.628
Total physicians per 100,000	147.49	119.15	0.067
Primary care physicians per 100,000	77.34	73.36	0.025
Opioid Rx rate per 100	59.64	44.74	0.291
Hospital beds per 1,000 population	7.00	8.94	-0.142
Percent non-Hispanic Black	10.42	6.92	0.162
Percent Hispanic	9.34	10.34	-0.048
Percent age 18–44	29.28	27.98	0.220
Poverty rate (%)	16.10	15.26	0.097
Uninsured rate (%)	12.77	13.17	-0.056
Median household income ($)	52597.59	52331.40	0.017
Rural-Urban Continuum Code	6.02	7.28	-0.370
Heroin death rate per 100,000	0.06	0.05	0.103
Non-synthetic drug OD rate per 100,000	2.10	1.64	0.245

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Table A10 – *continued*

	Matched controls	Never-treated pool	Norm. diff.
Interstate highway in county (0/1)	0.36	0.24	0.195
Acute escalation (N matched = 945, N never-treated = 541)			
Patients per 100,000 (time-avg.)	188.36	81.49	0.295
Log population	9.77	8.80	0.750
Total physicians per 100,000	146.12	123.47	0.041
Primary care physicians per 100,000	77.37	77.92	-0.003
Opioid Rx rate per 100	55.99	41.38	0.298
Hospital beds per 1,000 population	6.96	10.49	-0.238
Percent non-Hispanic Black	10.13	6.07	0.189
Percent Hispanic	9.42	11.06	-0.077
Percent age 18–44	29.00	27.64	0.237
Poverty rate (%)	15.87	15.05	0.093
Uninsured rate (%)	12.91	13.58	-0.092
Median household income ($)	53312.97	52283.35	0.063
Rural-Urban Continuum Code	6.09	7.69	-0.481
Heroin death rate per 100,000	0.07	0.04	0.171
Non-synthetic drug OD rate per 100,000	2.01	1.53	0.255
Interstate highway in county (0/1)	0.36	0.21	0.242
Sustained entry (N matched = 977, N never-treated = 1,154)			
Patients per 100,000 (time-avg.)	241.24	103.52	0.336
Log population	9.99	9.24	0.571
Total physicians per 100,000	161.07	122.11	0.080
Primary care physicians per 100,000	80.81	72.11	0.049

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Table A10 – *continued*

	Matched controls	Never-treated pool	Norm. diff.
Opioid Rx rate per 100	62.64	47.47	0.294
Hospital beds per 1,000 population	6.57	8.35	-0.151
Percent non-Hispanic Black	9.70	8.21	0.069
Percent Hispanic	9.02	10.16	-0.057
Percent age 18–44	29.62	28.41	0.198
Poverty rate (%)	16.14	15.85	0.034
Uninsured rate (%)	12.66	13.43	-0.110
Median household income ($)	52588.23	51874.87	0.044
Rural-Urban Continuum Code	5.95	7.05	-0.316
Heroin death rate per 100,000	0.07	0.05	0.132
Non-synthetic drug OD rate per 100,000	2.19	1.78	0.214
Interstate highway in county (0/1)	0.37	0.26	0.179

Notes: County-level time-averages across the full panel (2013–2023), same covariate list and normalized-difference formula (Imbens & Rubin 2015) as Table 2. Matched controls: counties selected as matched controls in the main matched CS-DiD design. Never-treated pool: counties that never cross the given shock's threshold at all – the permanent (time-invariant) subset of the larger, time-varying not-yet-treated comparison pool used in Table A9. Pre-period matching variables (pre-treatment mean/trend/SD) are not shown here, since they are defined relative to each county's own treatment date and have no counterpart for a permanently never-treated county; time-averaged patients per 100,000 is reported instead as the baseline-outcome-level analogue.

G. Dosing Robustness: Sublingual Formulations Only

Table A11 re-estimates Table 8 restricted to sublingual/film formulations, excluding the extended-release injectable formulations Sublocade and Brixadi, removing any noise introduced by the depot-injectable dose conversion described in Section 3.1.1. The pattern closely tracks the main dosing table: average daily dose and its MME equivalent rise significantly under acute escalation only, and the share of patients exceeding 16mg falls significantly under the same definition, while first occurrence and sustained entry show no significant change in average dosing. This confirms that the depot-injectable conversion is not responsible for the muted average-dose result in Table 8.

Table A11: Targeted Outcomes: Dosing, Sublingual Formulations Only

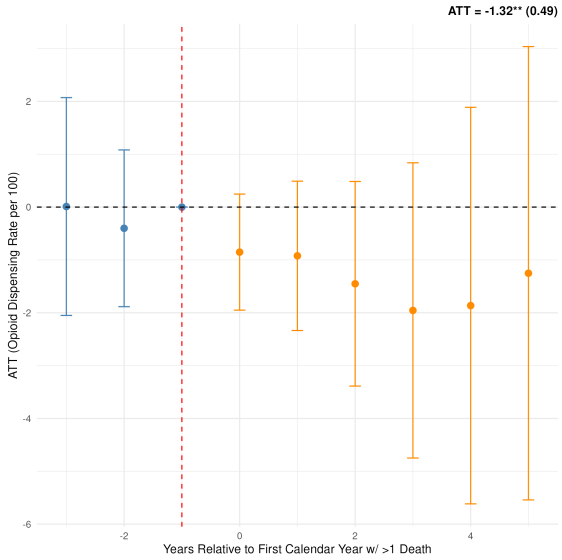
	(1)	(2)	(3)	(4)
	Avg. Daily Dose (mg)	Avg. Daily Dose (MME)	Share >16mg/day	Share >24mg/day
Panel A: First occurrence				
ATT	-0.007	-0.207	-0.001	0.003
	(0.051)	(1.533)	(0.003)	(0.002)
Pre-treatment mean	13.97	419.02	0.27	0.04
Percent effect	-0.05%	-0.05%	-0.46%	7.32%
Panel B: Acute escalation				
ATT	0.107*	3.212*	-0.006*	-0.001
	(0.049)	(1.485)	(0.003)	(0.001)
Pre-treatment mean	13.88	416.41	0.28	0.05
Percent effect	0.77%	0.77%	-2.21%	-1.82%
Panel C: Sustained entry				
ATT	0.053	1.581	0.003	0.003*
	(0.047)	(1.405)	(0.003)	(0.001)
Pre-treatment mean	14.06	421.65	0.27	0.04
Percent effect	0.38%	0.38%	1.02%	7.25%

Notes: Estimator: Callaway–Sant'Anna (2021), doubly robust, matched county-quarter panel, 5,000 bootstrap iterations, county-clustered SEs. Restricted to sublingual/film formulations, excluding Sublocade/Brixadi extended-release injectables (Section 3.1.1). $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

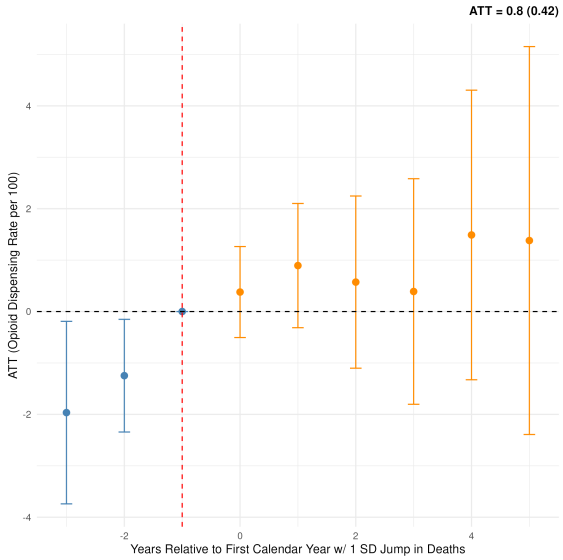
H. Opioid Analgesic Dispensing as a Secondary Outcome

Because the CDC series is annual, we collapse each shock definition to the calendar year of treatment onset and estimate the Callaway–Sant'Anna specification on a county-year panel, re-matched on the pre-shock trend in the opioid dispensing rate itself rather than reusing the buprenorphine-matched sample, and retaining the covariate adjustment used in the main analysis. The analytic sample covers 2013–2023, matching the coverage window of our main prescribing outcome. Standard errors are clustered at the county level via 5,000 bootstrap replications. Counties absent from the CDC series in a given year are treated as missing and not zero, since CDC reports approximately 98 percent of counties annually and non-reporting reflects data suppression, not an absence of dispensing.

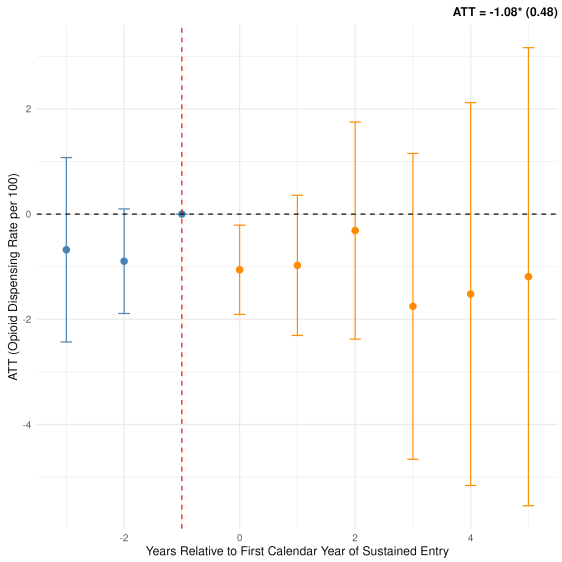
Table A12 reports the results. Opioid analgesic dispensing declines significantly following synthetic opioid shock onset under the first-occurrence (-1.32 prescriptions per 100 residents, SE $= 0.49$, a 1.7 percent decline relative to the pre-treatment mean) and sustained-entry (-1.08, SE $= 0.48$, 1.3 percent) definitions. The acute-escalation estimate is small, positive, and not statistically significant (0.80, SE $= 0.42$). Figure A8 presents the corresponding event studies.



(a) First Occurrence



(b) Acute Escalation



(c) Sustained Entry

Figure A8: Event-Study Estimates: Opioid Analgesic Dispensing Rate

Notes: Outcome is opioid analgesic prescriptions dispensed per 100 residents per year (CDC Opioid Dispensing Rate Maps, annual county-year panel), not morphine milligram equivalents. Treatment collapsed to the calendar year of onset. Matched sample re-estimated on the outcome's own pre-shock trend (Section H). Blue = pre-treatment; orange = post-treatment. Bars = 95% CIs. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.

Table A12: Average Treatment Effect on the Treated: CDC County Opioid Dispensing Rate

	(1) First Occurrence	(2) Acute Escalation	(3) Sustained Entry
ATT	-1.32**	0.80	-1.08*
	(0.49)	(0.42)	(0.48)
Pre-treatment mean	80	76	83
Percent effect	-1.66%	1.06%	-1.31%
Treated counties	1586	1719	1536
Comparison counties	1032	1000	1062
County-year obs.	34,421	37,148	33,492
Estimator	Callaway–Sant'Anna (2021), doubly robust		
SE clustering	County, 5,000 bootstrap iterations		

Notes: Outcome is the CDC county-level opioid dispensing rate (annual, county-year panel, 2013–2023). Matched sample: counties re-matched on opioid_rate's own 3-year pre-shock trend (mean/trend/SD), not the bup-prescribing match used in Table 4. $^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$.